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Results of computed tomographic coronary angiography in comparison with the table of pretest probability of chronic coronary syndrome

Aim To compare results of computed tomography coronary angiography (CTCA) with a table of pretest probability of chronic coronary syndrome (CCS) taking into account the following key variants: abnormality, microvascular damage, nonobstructive or obstructive atherosclerotic damage.

Material and methods 50 patients (39 men, 20 women) aged 30 to 67 years were evaluated with a computed tomography scanner PHILIPS Brilliance iCT SP 128. A high pretest probability of ischemic heart disease was found in 44% of cases and medium in 40%.

Results According to CCS data, coronary artery (CA) pathology was not found in 28% of patients. CA hypoplasia was observed in 4% of patients. 22% of patients had muscular bridges narrowing the CA lumen during systole by 40–50%. In 26% of cases, CA had minimal and early stenoses. Moderate and pronounced stenoses were observed in 20% of cases. In one case, there was a total occlusion of the circumflex branch. Calcinates were found in 9.1% of patients with muscular bridges, in 61.5% of patients with minimal and early stenoses, and in 80% of patients with moderate and pronounced stenoses. In the group with «clean» CA and congenital defects, calcinates were absent. The mean value of pretest probability was the highest in the patient group with moderate and pronounced stenoses, 22.5±13.13. It was significantly higher than in the group with muscular bridges (p=0.045) and congenital pathology of CA (p=0.01). At the same time, this value did not significantly differ from the group with «clean» CA and the group with minimal and early stenoses. Based on the study results, 2 bypass surgeries and 5 CA stentings were performed.

Conclusion Thus, the table of pretest probability of ischemic heart disease does not provide a differential diagnosis and evaluation of the nature of CA damage as compared to results of CTCA.

Keywords Computed tomography coronary angiography; invasive coronary angiography; chronic coronary syndrome; pretest probability; muscular bridge; coronary artery stenoses

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Diagnosis of coronary artery disease (CAD) involves conventional invasive coronary angiography (ICA) and non-invasive computed tomography angiography (CTA) [1, 2]. ICA is the gold standard for the diagnosis of CAD due to its excellent resolution in coronary artery imaging for catheter or surgical interventions [3]. ICA death is quite rare, but various cardiac and extracardiac complications are common [4].

Over the past decades CTA has become an effective non-invasive technique of coronary imaging [5, 6]. Radiation exposure has been reduced, and advanced scanners can perform CTA with a radiation load of 2–3 mSv. As a result, more and more health care providers worldwide apply CTA [7].

CTA provides a high-quality assessment of coronary lesions and quantification of atherosclerotic plaques in the vessel walls. The introduction of multislice computed tomography (MSCT), such as 64-, 128-, 256-, and 320-slice MSCT, has ensured high diagnostic accuracy of CTA [8].

However, applying CTA still involves some challenges. These techniques can not be used in patients with rapid atrial flutter and atrial fibrillation, high Agatston scores (≥600), severe kidney dysfunction, and iodine allergy [9]. Severe calcification is the main limitation of obtaining CT images of high quality [10].

In patients with acute coronary syndrome CTA is less informative than virtual-histology intravascular ultrasound in assessing plaque stability [11, 12]. At the same time, further investigation of annular opacity around a plaque, and internal irregularities of plaque will allow CTA to identify patients at high risk of developing severe coronary complications [10]. Further studies are required to assess the functional significance of stenosis using the intravascular gradient of contrast attenuation [13, 14].

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Ischemic depression of the ST-T segment in Holter electrocardiogram (ECG) is a poor predictor of sudden cardiac death and has low rates in confirming coronary stenosis. Nevertheless, ambulatory Holter ECG remains one of the most accessible investigations and is widely used in all patients with pain syndrome.

As a result, many changes are found at the end of the ventricular complex which are not always confirmed by clinical symptoms, but must be explained in the diagnosis. Stress tests are performed only in certain outpatient treatment facilities. Moreover, the comparison of the diagnostic efficacy of CTA and conventional exercise stress investigation in patients with low to medium pretest probability of CAD has showm that CTA had a significant advantage over functional stress tests in the ability to predict cardiovascular complications [15, 16]. Stress echocardiography can be performed only in hospitals. Thus, there is a need in outpatient practice for a universal and accessible technique which will determine whether a patient has coronary disease or transient ST-T segment depression in the ECG due to other reasons.

Aim

To match CTA results with the chronic coronary syndrome (CCS) pretest probability table concerning anomalies, small vessel disease, non-obstructive or obstructive disease.

Material and methods

The study included 50 patients (30 males, 20 females) from 30 to 67 years of age. The mean age was 51.62±8.98 years.

The study was conducted between January 2019 and August 2020. The inclusion criteria were as follows:

1) typical pain syndrome without ischemic ST-T segment depression according to bicycle ergometry or Holter ECG;
2) atypical pain and/or dyspnea with transient ST-T depression according to bicycle ergometry or Holter ECG;
3) asymptomatic transient ST-T segment depression shown by bicycle ergometry or Holter ECG;
4) regional hypokinesia in echocardiography without a history of myocardial infarction (MI) and scarring in ECG.

Exclusion criteria: documented history of MI, typical pain or dyspnea with transient ST-T segment depression according to bicycle ergometry or Holter ECG. Patients meeting the exclusion criteria were immediately hospitalized for ICA. The study did not include patients younger than 18 years of age, pregnant women with a history of intolerance of iodine-containing contrast agents, patients with chronic kidney disease stage 3B or higher with unstable hemodynamics, or left ventricular ejection fraction <35%.

The study was conducted following the ethical principles of the Declaration of Helsinki of the World Medical Association. All patients signed the informed consent to undergo CTA and ICA. The relevant approval was granted by the ethics committee.

Prior to the beginning of the study, CAD pretest probability and additional determinants of the clinical likelihood of coronary artery disease were evaluated. The main anthropometric measurements were performed: height, body weight, body mass index, waist circumference, and hip circumference. All patients were subjected to ECG, echocardiography, conventional Holter ECG, bicycle ergometry, or treadmill test, if not contraindicated. Eligible patients underwent CTA. The results of CTA were compared with the evaluation of pretest probability.

All patients examined had a sinus rhythm. Patients with a heart rate >70 bpm took metoprolol 50 mg once, 45 minutes prior to the scan, if not contraindicated.

The scan was performed in a 128 slice CT scanner (PHILIPS Brilliance ICT SP 128) in breath-holding spells, with prospective ECG gating within 70–80% of the R-R interval. During a single rotation of the X-ray tube, 128 slices 0.5 mm thick were made simultaneously.

At the beginning of the investigation, topography was performed in the lateral and frontal views. These were used as the boundaries of the area of interest (from the trachea bifurcation to the inferior border of the heart). CTA was performed with intravenous administration of 80 mg of non-ionic iodine-containing contrast agent (350 mg of iodine/mL) at the rate of 5 mL/sec with an automatic syringe. The exam started automatically when an X-ray density of 300 HU was achieved in the descending aorta lumen.

ICA was performed within 1 month after CTA, if necessary

The axial CT images of the arterial bed were studied. Coronary artery lumen was evaluated segment by segment according to the classification of the Society of Cardiovascular Computed Tomography (SCCT) [17, 18]. The degree of stenosis was assessed using the classification suggested by the SCCT:

- 0 – no stenosis;
- 1–24% – minimal stenosis or plaque with no stenosis. Minimal non-obstructive CAD;
- 25–49% – mild stenosis. Mild non-obstructive CAD;
- 50–69% – moderate stenosis. Consider functional assessment.
- 70–99% – severe stenosis. Consider ICA or functional assessment;
- Left main >50% or 3-vessel obstructive (≥70%) disease. ICA is recommended;
- 100% stenosis (total coronary occlusion). Consider ICA and/or viability assessment.

Only good and excellent quality images were used. All arteries of a diameter greater than 2.0 mm were analyzed.

According to Holter ECG, 37.2% of patients referred to CTA had atypical pain syndrome with ischemic ST-T segment depression. Painless myocardial ischemia was detected in 13.95% of patients. 46.51% of patients complained of typical angina attacks without ischemic changes on Holter ECG.

In 18.6% of patients examined, repolarization abnormalities were found on ECG at rest. Diffuse changes in the myocardium were detected in 13.95%, left ventricular hypertrophy in 23.3%, and intraventricular conduction abnormalities in 2.3% of cases. 27.9% of patients had normal ECG.

The increased thickness of intima-media >1.0 mm was found in 18.6% of cases. Brachiocephalic plaques were detected in 27.9% of cases, while 4.7% of patients had plaques in the lower extremity arteries.

Hypokinesia of individual myocardial segments was determined by echocardiography in 37.2% of cases.

The pre-test probability of CAD was evaluated for all patients using an online calculator [19]. Additional determinants of clinical probability of CAD were also assessed [20]. High CAD pre-test probability was found in 44%, an average probability in 40%, and probability in 16% of cases. All patients were distributed into groups was as follows. Group 1 included 11 patients with myocardial bridges. Group 2 consisted of 13 patients with minimal and mild stenosis. Group 3 included 10 patients with moderate and severe stenosis and total occlusion. Group 4 comprised 14 patients with clean coronary arteries. Group 5 included 2 patients with coronary artery anomalies.

The statistical analysis of the data obtained was performed using the Statistica 12.0 software suite. The data is presented in the table. The normality of trait distribution was tested using the Shapiro-Wilk W-test. The Mann-Whitney U-criterion was used to determine the significance of differences between the quantitative variables. Given the multiplicity of the comparison groups, one-way ANOVA was also used. The chi-squared test was used to compare qualitative variables [22]. The differences were considered statistically significant at $p<0.05$.

Results

The CTA findings of patients included in the study are shown in Table 1. Coronary pathology was not detected in 26% of cases. Coronary hypoplasia was found in 4% of cases. In 22% of cases myocardial bridges (MB) narrowing the lumen in systole by an average of 40–50% were found. Coronary artery calcification was detected in 34% of cases. It should be noted that it was found in 1 case (9.1%) in the group of patients with MB, in 8 (61.5%) patients with minimal and mild stenosis, and 8 (80%) patients with moderate and severe stenosis. Calcification was not detected in patients with clean coronary arteries and those with coronary artery anomalies.

In Group 2 (patients with minimal and mild stenosis) one case of minimal stenosis (1–24%) of the left anterior descending artery (LAD) was detected. There were no cases of minimal stenosis of the left circumflex artery (LCX) and the right coronary artery (RCA). Mild stenosis (25–49%) was detected in LCA in 1 (4.2%) case, LAD in 11 (84.6%) cases, LCX in 3 (23.1%) cases, and RCA in 5 (38.5%) cases.

In Group 3, moderate stenosis (50–69%) of LCA was found in 1 (10%) case. There were 2 cases of moderate stenosis in LAD (20%). Moderate stenosis of LCX was detected in 3 (30%) cases, moderate stenosis of RCA in 2 (20%) cases. Severe stenosis (70–99%) was detected in LCA in 2 (20%) cases, LAD in 11 (84.6%) cases, LCX in 1 (10%) case, and RCA in 3 (30%) cases. There was 1 case (10%) of LCX occlusion. In 1 (10%) case, severe stenosis was found in 3 vessels (LAD, LCX, and RCA simultaneously). Mild stenosis was found in Group 3, as well as moderate and severe stenosis: LAD in 11 (40%) cases, LCX in 3 (30%) cases, and RCA in 1 (1%) case. There was 1 case (10%) of minimal LAD stenosis.

In Group 3, 7 (70%) patients were referred for ICA due to the detection of severe stenosis. Based on the ICA results, coronary artery bypass grafting was performed in 2 cases and stenting of a coronary artery in 5 cases. In 2 cases ICA was performed due to the unclear image of LAD and LCX.

The analysis of the BM group determined that BMs were located most often in LAD (72.7%). The coronary artery lumen narrowed at the MB level by 40–50% in 27.27%, and by 30% and less in 63.63% of cases during myocardial contraction. The combination of BM and coronary stenosis was detected in 27.27% of cases. Mild stenosis of LAD and LCX was found in 3 (27.3%) and 2 (18.2%) cases, respectively.

The age of patients with BM did not differ significantly from that of patients in Groups 2 and 4. However, the former were significantly younger than patients in Group 3. There were more male patients (63.64%).

Typical and atypical pain syndrome was equally common, but patients did not have painless myocardial ischemia and dyspnea. The difference was significant with both Groups 2 and 3. Transient ST-T segment depression in the BM group was significantly more frequent than in Group 2. There was an insignificant difference between Group 3 and patients with clean coronary arteries was insignificant. This fact can be explained by the specific features of the transmyocardial course of coronary arteries, which causes them to squeeze with exercise. Clinical manifestations and changes on the ECG develop as a result, similar to those observed in hemodynamically significant coronary stenosis. The absence of a significant difference with clean coronary arteries is explained by microvascular coronary disease.

Male patients prevailed in Group 2 with minimal and mild stenosis (76.92%). Typical pain syndrome was almost equally frequent (38.5%), as was atypical pain syndrome (30.8%), and painless myocardial ischemia (30.8%). At the same time, the frequency of dyspnea (15.38%) was significantly higher

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Table 1. Comparative characteristics of patients depending on changes detected by computed tomography angiography

Parameter	Myocardial bridges, n=11 (1)	Minimum and mild stenosis, n=13 (2)	Moderate stenosis, severe stenosis, total occlusion, n=10 (3)	Clean coronary arteries, n=14 (4)	Coronary artery anomalies, n=2 (5)
Age, years	47.45±9.53	50.15±9.52	60±6.59 p_{1-3}= 0.003; p_{2-3}=0.01 p_{3-4}=0.001; P_A=0.006	49.93±6.53	54±0
Sex: • male • female	63.64% 36.36%	76.92 23.08	50% 50% p_{2-3}=0.049	57.14% 43.88%	0 100%
BMI, kg/m²	31.18±4.85	31.36±7.27	28.70±3.33	29.01±5.49	30.12±4.45
WC, cm	106.63±18.04	109.5±15.39	100.57±11.82	96.54±15.04	101±2.43
HC, cm	107. 63 ±9.18	110.8±15.04	106.86±8.71	106±7.85	116±3.47
Pain syndrome: • typical, % • atypical, % • painless ischemia, %	54.55 45.45 –	38.5 30.8 30.8 p_{1-2}=0.004	60 30 10	35.71 57.15 7.14 p_{2-4}=0.03	0 50 50
Dyspnea, %	0	15.38 p_{1-2}=0.001	10 p_{1-3}=0.001; p_{2-3}=0.285	0 p_{2-4}=0.001	0
Pretest probability, %	12.55±11.05	15.92±12.03	22.5±13.13 p_{1-3}=0.045	14.28±10.28	7.5±3.47 p_{3-5}=0.01
Pretest probability: • low <5% • moderate 5–15% • high >15%	27.27 36.36 36.36	15.38 46.15 38.46	0 30 70 p_{1-3}=0.029; p_{2-3}= 0.004	7.14 50 42.86 p_{3-4}=0.001	0 100 0
ECG: LVH, % repolarization abnormality, % diffuse myocardial changes, %	36.36 45.45 9.1	23.08 30.76 7.69	30 – 20	35.7 21.43 14.29	0 50 50
ST–T depression with stress test, %	36.36	7.69 p_{1-2}=0.01	30 p_{2-3}=0.04	35.7 p_{2-4}=0.009	50
IMT >0.9 mm, %	18.18	0	30	21.43	0
Brachiocephalic plaques, %	18.18	23.08	50 p_{1-3}=0.03	14.29 p_{3-4}=0.007	0
Hypokinesia zones according to echocardiography, %	36.36	46.15	30	35.71	0

The data is expressed as the mean and the standard deviation (M±SD).
PA – significant difference calculated using one-way ANOVA; p_{1-2} – significant difference between Groups 1 and 2; p_{1-3} – significant difference between Groups 1 and 3; p_{1-4} – significant difference between Groups 1 and 4; p_{2-3} – significant difference between Groups 2 and 3; p_{2-4} – significant difference between Groups 2 and 4; p_{3-4}– significant difference between Groups 3 and 4. BMI, body mass index; WC, waist circumference; HC, hip circumference; ECG, electrocardiogram; LVH, left ventricular hypertrophy; IMT, intima-media thickness.

than in the groups of patients with BMs, clean coronary arteries, and moderate and severe stenosis. The mean pre-test probability in all groups did not differ from that in the BM group and patients with clean coronary artery, but significantly lower than in the group with hemodynamically significant stenosis. Patients with moderate pre-test probability (46.15%) prevailed.

The frequency of hypokinesia did not differ between the groups according to echocardiography. Three-vascular coronary disease (LAD, LCX, and RCA) was found in 7.69% of cases, two-vascular disease in 38.46%, and there was 1 case of LCA stenosis. Coronary artery calcification was detected in 61.54% of cases.

Older age is a characteristic feature of patients with moderate and severe coronary stenosis (Group 3). Patients in group 3 were significantly older than in other groups. There were significantly more female patients in Group 3 than in the group with minimal and mild stenosis. The predominance of typical pain syndrome (60%) was also a characteristic feature. Atypical pain syndrome was found 2 times less often (30%), but painless episodes were observed in 10% of cases. There were more patients with high pre-test probability (70%). The yield of high pre-test probability was significantly higher than in the remaining four groups. Low pre-test probability was not found in patients with moderate and severe coronary stenosis.

Transient ischemic ST-T segment depression was observed in 30% of cases. This was significantly more frequent than in the group with minimal and mild stenosis. This was due to less severe coronary atherosclerosis in Group 2. The difference between Groups 1 and 4 was insignificant. Carotid plaques were significantly more frequent (50%) in the group with moderate and severe coronary stenosis than in Groups 1 and 4.

The frequency of painless myocardial ischemia was significantly higher in patients with clean coronary arteries than in comparison with Group 2. The former had no dyspnea, more frequent ischemic ST-T segment depression with exercise than in Group 2. They also had a lower incidence of plaques compared to the group with moderate and severe stenosis. Ischemic depression without coronary disease was due to microvascular disease and mitral valve prolapse in 1 case.

Discussion

The study demonstrated that CTA allowed not only identifying patients with at risk of coronary complications but performing differential diagnosis in ambulatory conditions without ICA. Our study identified many patients with BMs (22%). According to the literature, there are significant differences in the detected frequencies of BMs. Japanese research revealed transmyocardial course of coronary arteries in 57 (30.3%) of 188 patients with CAD [21]. MBs were found in 336 of 2,462 patients with CAD (13.6%) in the Chinese population [22] and in 22.5% of patients with CAD in Saudi Arabia [23]. The prevalence of BMs varies significantly from 3.5 to 58%. This wide variation can be explained by different generations of CT systems used in the studies. Those with faster acquisition requiring shorter breath-holds, artifacts and misinterpretations are significantly less frequent [24]. As seen in the literature, the probability of detecting BM is higher for CTA than for conventional ICA [25].

In our study the need for ICA after CTA was low. This saved extra costs associated with hospitalization and possible complications caused by the invasive procedure [5]. The cost per patient with a true positive diagnosis was reduced in the economic model of health care system. Using ICA as a reference standard, CAD pre-test probability was up to 70% and lower than that of CTA. With a CAD pre-test probability of 70% or higher, ICA was associated with a lower cost per patient with a true positive diagnosis [25].

Coronary atherosclerosis, which required treatment, was identified in 4 cases with low pretest probability. In 28% of cases, transient ST-T segment depression was not confirmed by CTA and was caused by microvascular coronary disease (26%) and mitral valve prolapse in 1 (2%) case. There were no plaques and coronary artery anomalies in 6 (12%) patients with a high pretest probability of CAD.

Conclusion

Thus, the table of pretest probability of ischemic artery disease does not help in differential diagnosis and assessing coronary artery disease when compared with computed tomography angiography findings.

No conflict of interest is reported.

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