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Original Article

CORONARY COMPUTED TOMOGRAPHY ANGIOGRAM IN PATIENTS WITH STABLE CHEST PAIN

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Summary

Using CT in patients with stable angina can help diagnose obstructive and non-obstructive coronary heart disease and improve the prognosis of patients. Purpose of this study was to compare the diagnostic accuracy of CT in patients with stable angina to conventional invasive angiography. A retrospective study of 142 consecutive patients with stable angina from 2005 to 2014 was conducted. All patients underwent CT coronary angiography and subsequent conventional angiography. Patients without significant stenosis but with typical anginal symptoms and over three risk factors for coronary heart disease, such as after PCI and ACB, and patients with CT evidence of significant coronary atherosclerosis were also included in this study. A contingency table was used to calculate sensitivity and specificity. The value of the cap was 0.610. The sensitivity of the methodology was 93% (CI 89% - 98%), the specificity 57% (CI 89% - 98%), the positive predictive value was 88%, and the negative predictive value was 73%. The high sensitivity, negative and positive predictive hundredth of CTA compared to conventional angiography suggest that this methodology is of great diagnostic value and opportunities to influence the clinical behavior and improve the prognosis.
Keywords: computed tomography angiography, invasive angiography, stable angina.

Introduction

The most common application of computed tomography angiography (CT) is the evaluation of patients with suspected cardiovascular disease. When complaints are chronic and related to a particular provocative moment, such as emotional stress or physical exertion, they are categorized as „stable." In these cases, this methodology can help diagnose both obstructive and non-obstructive coronary heart disease and improve the accuracy of the diagnosis and prognosis of patients. Appropriate patient selection is essential to achieve optimal images for research and the best diagnostic accuracy.

Although older recommendations suggest that CT could be the most effective in low- and

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intermediate-risk patients, it is noteworthy that most algorithms overestimate the likelihood of obstructive coronary heart disease [1,2,3]. Recent European and US recommendations provide an appropriate algorithm for assessing the risk of coronary heart disease, derived from 15,815 symptomatic patients, based on age, sex, and symptoms. When this algorithm is applied, 50% of the risk group are males over 70 years old with chest pain, even though 52% or less develop obstructive coronary heart disease.

Other recent risk scales have shown an even lower risk of coronary heart disease [4], further supporting the claim that hazard rates alone are insufficient to identify patients with a really high risk of coronary heart disease.

The 2021 AHA / ACC recommendations for chest pain indicate that, in stable angina and low risk of obstructive coronary heart disease (e.g., <15%), additional testing may not be necessary. However, intermediate or high-risk patients may benefit from additional diagnostic tests such as CT or functional testing. The severity of underlying coronary calcification may be critical in identifying patients at high risk for obstructive coronary heart disease [4]. Accordingly, previous CT scans for coronary calcium should be reviewed and evaluated when possible.

The absence of Ca favours conducting a CT scan, while its presence suggests a functional study.

Materials and Methods

A retrospective study of 142 consecutive patients with stable angina, hospitalized or examined from 2005 to 2014 was conducted. All patients underwent CT coronary angiography and subsequent conventional angiography. Patients without significant stenosis but with typical anginal symptoms and over three risk factors for coronary heart disease were also included in this study, such as those after PCI and ACB and patients with CT evidence of significant coronary atherosclerosis. In 10 patients, CT angiography and subsequent coronary angiography were performed due to another indication other than chest pain – upcoming heart surgery, planned major surgery requiring risk determination, and dilatative cardiomyopathy (DCMP).

Selection of suitable candidates for coronary tomography angiography

Although CT scans have great potential for determining the amount and severity of coronary heart disease, similar to other imaging techniques, the accuracy and effectiveness of the method depend on the selection of patients in whom high-quality imaging can be achieved. The use of modern devices with improved temporal and spatial resolution contributes to achieving optimal image quality. For example, dual-tomography tomographs allow imaging in patients with higher heart rates due to improved time resolution. Tomographs with better spatial resolution improve the image, especially in the presence of calcium. Patients who are good candidates for CT scans have no proven coronary heart disease, can maintain a low heart rate (e.g., 70 bpm with medication), can hold their breath while receiving the image, and can tolerate contrast material. A smaller number of patients was used in this study, with 16 section tomograph and the predominant number of 320 slices of computer tomography.

Statistical analysis

A contingency table was used to calculate sensitivity and specificity, in which the frequencies of the individual variables are plotted. It presents the main interaction between the individual variables and serves to detect the relationship between them.

We used Cohen's in the data analysis and kappa coefficient to measure the consistency of the two qualitative methods. This approach is considered more reliable than calculating the percentage, as it considers the random consistency of the two methods. The method measures the consistency between two methods that have classified N values in C into some mutually exclusive categories. The Kappa coefficient is defined as:

$$k = \frac{P_0 - P_e}{1 - P_e} = 1 - \frac{1 - P_0}{1 - P_e}$$

where "p_0" is the observed relative agreement between the qualitative methods, "p_e" is the theoretical probability of random agreement, using the collected data to determine the probability of random distribution in the categories. If the two qualitative methods are in complete agreement, then Kappa is equal to 1. If there is no agreement, Kappa is less than or equal to 0.

The following Table 1 is used to interpret Kappa:

Table 1. Interpretation of Kappa values

	Interpretation
<0	No consent
0.0-0.19	Weak consent
0.20-0.39	Satisfactory consent
0.40-0.59	Moderate (medium) consent
0.60-0.79	Significant (large) consent
0.80-1.00	Almost complete agreement

Specificity and negative predictive value were calculated based on cross-tabulation.

Sensitivity – the proportion of well-defined true positive cases and specificity - the proportion of well-defined true negative cases are calculated. Sensitivity does not include false negatives, but specificity does not include false positives.

A positive predictive value is a ratio between true positive results and the sum of all positive results. The formula used to calculate the negative predictive value of the methodology is similar.

Positive predictive value is not inherent in the test. It depends strongly on the prevailing case. For example, if a property is true for everyone in a group, then PPV would be 100%, and NPV would be 0%. Therefore, its property is proposed to normalize the PPV approach to a prevalence of 50%. This was not done in the present study, as the data allowed adequate calculation of negative and positive predictive values.

Results

The main characteristics of the studied population

We studied 213 patients with a mean age of 61 years (age range 33-93, Table 2).

In the studied population, the tendency for the predominance of men is impressive, as most of the cases belonged to the age group > 55 years. Risk factors predominated - arterial hypertension and dyslipidemia, followed by familial pregnancy and smoking. Diabetes mellitus was present in 25.8% of the studied patients, of which 15 (7% of the general population) were on insulin therapy, 26 (12.2%) were on oral therapy, and 14 (6.5%) were on diet therapy. 27 (12.6%) patients had chronic renal failure.

Table 2. Main risk factors distribution

	Number
Total patients	213
Men	158 (58.6%)
Hypertension	206 (96.7%)
Dyslipidemia	196 (92.01%)
Smoking	78 (36.6%)
Family burden	85 (39.9%)
Diabetes	55 (25.8%)
Obesity	31 (14.5%)
Generalized atherosclerosis	18 (8.4%)
Chronic renal failure	27 (12.6%)
Age≥55 years	159 (74.6%)

Distribution of patients by several risk factors

The study group included patients with an average of 4.6 risk factors for coronary heart disease: defined as gender, age, hypertension, dyslipidemia, smoking, diabetes, obesity, and generalized atherosclerosis (Table 3). Two patients included in the analysis had two risk factors but were included in the analysis due to objective data for preceding revascularization.

Table 3. Average number of risk factors per patient

	Value
Average	4.6808
Standard deviation	1.22531

Clinical indicators

It can be seen that the majority of patients had stable angina – 68%, unstable patients were a significantly smaller group, mainly in the low-risk and intermediate-risk range of unstable angina, with negative enzymes for myocardial necrosis. A small percentage of the patients had atrial fibrillation, which is why reaching the target heart rate of <70 beats/min is difficult in this group (Table 4). About 47% of the studied population underwent revascularization, and 2/3 had interventional revascularization.

Table 4. Clinical indicators

Clinical characteristics	Number (%)
Unstable angina	57 (26.7%)
Stable angina	146 (68.5%)
Atrial fibrillation	11 (5.1%)
Previous PCI	67 (31.4%)
Previous ACB	34 (15.9%)

Number of affected vessels in the study group

It can be seen that the main group of patients studied had one-vessel coronary artery disease – approximately 34%, followed by three-vessel patients – 29.7% (Figure 1). Two-vessel disease patients accounted for 18.87%, with the lowest number of patients without evidence of coronary atherosclerosis - 17.45%. There was significant stenosis in 38 (17.8%) patients.

Distribution of patients by year of CT

From 2005 until July 23, 2009, the computer tomograph used for coronary CT angiography was the GE LightSpeed 16 Slice CT, and from September 17, 2009, until today, it is the Toshiba AquilionOne 320-slice CT (Figure 2).

It can be seen that the highest percentage of the examined patients was in 2010, as the percentage of performed CT angiographies increased significantly after the replacement of the 16-slice computed tomography with a higher-tech one. The distribution of the examined patients was a relatively stable value from 2009 to 2013. In 2014, it was lower, as the patients included in the study were those examined in the clinic until June 2014.

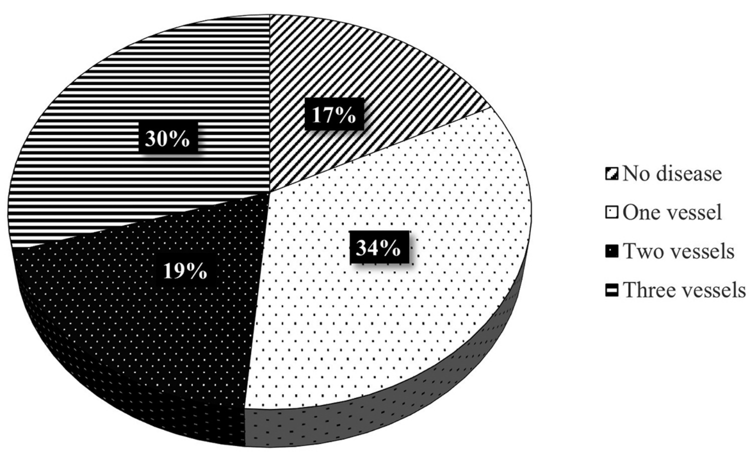

Figure 1. Percentage distribution of patients by number of affected vessels

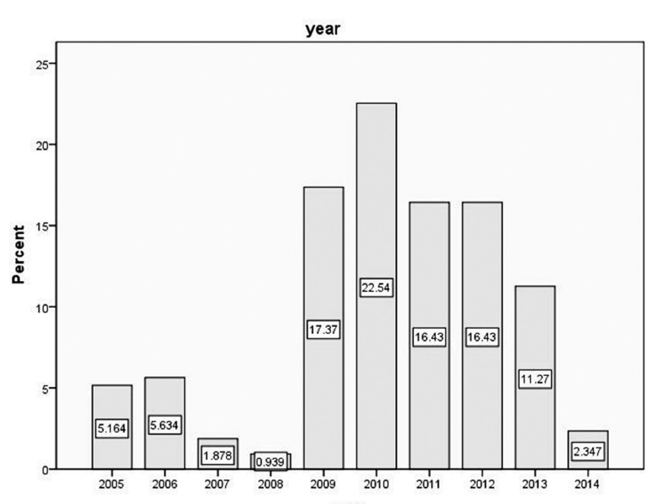

Figure 2. Percentage distribution of the examined patients according to the year of the performed CT

When performing CT angiography, the presence of calcium in the coronary arteries was determined (Figure 3). In severe calcinosis, CT examinations were not performed. In these cases, calcium makes the image interpretation impossible while being an indicator of high risk, and the patient underwent conventional angiography. When assessing a segment of the coronary circulation was difficult, it was usually noted in the image interpretation.

Stable angina

It is defined as the appearance of angina symptoms with similar physical exertion or the equivalent of angina - shortness of breath, easy fatigue with similar efforts, without complaints at rest. The coincidences were noted in the table below when examining patients with stable angina (Table 5).

The value of Kappa was 0.610, suggesting broad consent (Table 6).

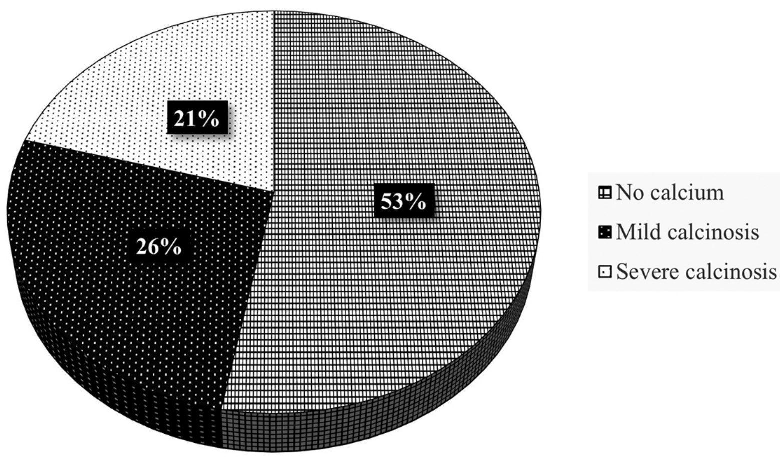

Figure 3. Percentage distribution according to the presence calcium in the coronary arteries. The majority (53%) have no calcium

Table 5. Crostabulation - stable angina

0			SCAG				TOTAL NUMBER
			2	3			
1							
CTA	0	number	18	5	0	2	25
		% of SCAG	56.3%	11.4%	0.0%	5.3%	17.6
	1	number	12	30	7	2	50
		% of SCAG	37.5%	68.2%	25.0%	2.6%	35.2%
	2	number	1	7	21	3	32
		% of SCAG	3.1%	15.9%	75.0%	7.9%	22.5%
	3	number	1	2	0	32	35
		% of SCAG	3.1%	2.7%	2.5%	84.2%	24.6%
Total number		number	32	44	28	38	142
		100.0%	100.0%	100.0%	100.0%	100.0%	
% of SCAG							

(0) patients with no disease
(1) patients with one vessel disease
(2) patients with two vessel disease
(3) patients with three vessel disease
Horizontal plane – based on selective coronary angiogram (SCAG)
Vertical plane – based on computer tomographic angiography (CTA)

Table 6. Statistics - stable angina. Confidence interval of Kappa

		Value	Rev.	Std. Error	95% Confidence Interval	
				Lower	Upper	
St. of consent	Kappa	, 610	-, 002	, 052	, 506	, 706
Number of valid cases		142	0	7	128	155

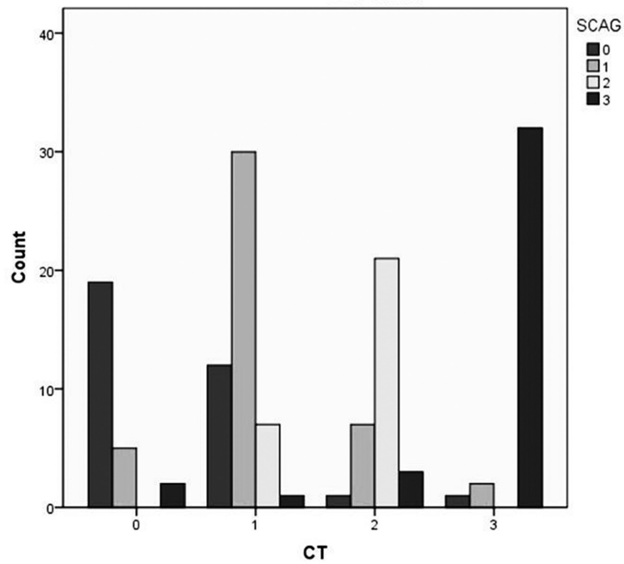

Figure 4. Distribution of patients by number of affected vessels in relation to CT and SCAG in stable angina

In the sample population, with a 95% degree of certainty, the Kappa was expected to be in the range of 0.506 ÷ 0.706. The sensitivity of this methodology is 93% (CI 89% -98%), the specificity is 57% (CI 89% -98%). The positive predictive value was 88%, and the negative predictive value was 73%.

Figure 4 shows that the discrepancy between the two methods was observed mainly in one-vessel patients and those without coronary atherosclerosis. Again, both methods can identify two- and three-vessel patients.

Discussion

Schmermund et al. examined 706 patients and followed them for 3.2 years. None of those with normal coronary vessels who developed myocardial infarction underwent a subsequent revascularization procedure or were registered with cardiovascular death (negative predictive value 100%). Of those with <50% lumen stenosis, 96% had no follow-up MACE on follow-up [5]. In another follow-up of 376 patients with no evidence of coronary atherosclerosis over three years, Fazel et al. also did not report the presence of MACE - myocardial infarction, cardiovascular death, or coronary intervention [6]. In our study, the negative predictive value of the methodology was calculated not based on MACE but invasive coronary angiography findings.

Results after coronary computed tomography angiography

Several controlled, randomized trials compared CT scans with functional tests in patients with stable angina. These studies assessed the importance of CT for diagnosis, symptomatology, risk stratification, clinical behavior, and patient prognosis.

SCOT-HEART (Scottish Computed Tomography of the HEART) is a prospective, randomized, multicenter study of 4146 patients on standard therapy and CT or standard treatment alone. Conducting a CT scan reduces the diagnosis of angina caused by cardiovascular disease.

The CAPP (Cardiac ST for the Assessment of Patients with Pain and Plaque) and the CRESCENT study [7, 8] were structured to assess the importance of CT in anginal pain compared to functional testing. The use of CT is associated with lower levels of angina after 12 months of follow-up. Similar results were observed in the

SCOT-HEART study, especially in patients with normal coronary arteries or obstructive coronary heart disease who underwent revascularization [9].

SCOT- HEART and PROMISE are the most extensive studies to date, assessing the importance of CTA for the clinical approach. The SCOT-HEART study is a prospective, multicenter study of 4,146 patients with stable angina from 12 centers in Scotland who were randomized to standard behavior and in addition to CT or standard treatment alone (including 85% stress test), which were rare (9%). The mean follow-up was 4.8 years, with additional CT leading to a 41% reduction in the combined endpoints of cardiovascular (CV) death and non-fatal myocardial infarction (MI) (2.3% vs. 3.9%; HR 0.59; P = 0.004).

The PROMISE study compared the strategy of CT with a functional study (67/5 nuclear stress test, 27% stress echocardiography, 10% stress test). The primary endpoints were death, MI, hospitalization for unstable angina, or a major procedural complication. At follow-up of 25 months, 164 patients (3.3%) in the CT scan group and 151 (3.0%) in the functional test group reached the primary endpoint (HR 1.04, P = 0.75). Although no difference in primary endpoints was observed, CT was associated with a lower incidence of death and MI at 12 months of follow-up (HR 0.66; P = 0.049). It is also associated with a lower incidence of obstructive coronary heart disease with invasive coronary angiography 90 days after randomization (secondary endpoint). During this period, however, more patients in the CT scan group underwent invasive coronary angiography (12.2% vs. 8.1%), and more patients in the CT scan group were revascularized (6.2% vs. 3.2%). The shortcomings of the study include a higher frequency of events, with a total of 315 (800 are considered to have reached 90% certainty and a 20% reduction in events). The study used a pragmatic design to generalize the results. Therefore, the specific center determined the decision for a given patient without guidelines for researchers.

An accurate follow-up analysis of PROMISE examined cardiovascular outcomes in 2,144 patients with diabetes. Patients with diabetes who underwent CT scans had a lower risk of cardiovascular mortality and MI than those randomized to functional tests (CT scan 1.1% vs. 2.6%, HR 0.39; P = 0.01) [10].

Several additional non-randomized trials suggest that CT may be associated with a lower incidence of events. A metaanalysis examined major cardiovascular events after the CTA, compared to the usual approach, and included the results of the PROMISE study, SCOT-HEART - the initial follow-up results of 1.7 years, and the CAPP study. In the metaanalysis, the application of CTA was associated with a 30% reduction in MI (HR 0.69 (95% CI, 0.49-0.98) [11]. A similar reduction in MI was observed in the large (n = 86,705) observational Danish Register (HR 0.71 (95% CI, 0.61-0.82)) [12]. The lower risk of MI was similar when comparing patients undergoing the treadmill stress test and SPECT MPI.

In the follow-up, we did not analyze MACE in the studied group of patients, as the study aimed to directly compare two anatomical methods in patients with intermediate risk. There are many studies worldwide, some of which have been described below and demonstrate this methodology's clinical and economic benefits. In invasive angiography, the functional significance of the lesions is also important, given their predictive value for MACE. The functional assessment of lesions based on CT diagnostics is not yet widespread in Bulgaria and is the subject of numerous studies worldwide. There is also still a debate about the functional methods of examination based on conventional angiography - FFR, iFR.

Mechanism of better results

The main issue is the mechanism of the improved forecast after the CTA. Studies like PROMISE, SCOT-HEART, and the Danish registry, which compare CTA with functional tests, have shown that CTA is associated with more frequent use of statins and aspirin. Other registries corroborated these data by showing a stepwise increase in preventive therapy when more severe coronary heart disease than CT was detected [12]. At five years of follow-up by SCOT-HEART, a higher incidence of statins and antithrombotic drugs was observed, which persisted over time. In addition, the observed reduction in events was explained by the benefits of drug therapy [13]. The PROMISE study also demonstrated the importance of preventive therapy, where a large percentage of events in patients randomized to functional examination were seen in the group without any changes [14]. Although some researchers have suggested that a higher incidence of revascularisation in the CTA group leads to fewer events, there is still no evidence that revascularisation is associated with an improved prognosis.The main drawback of CT is that it can lead to more invasive coronary angiography and coronary revascularization. The PROMISE study observed an approximately 50% higher incidence of invasive coronary angiography and a two-fold increase in revascularization with CT. No significant differences were observed in the SCOT-HEART study, but the absolute frequency of revascularization was higher than PROMISE (10.5% vs. 4.7%). In the SCOT-HEART study, the initial incidence of invasive coronary angiography and coronary revascularization was higher in the CTA group but subsequently levelled off within five years. In fact, after 12 months, the incidence of invasive coronary angiography and coronary revascularization was higher in the standard approach group. This suggests that despite the initially increased incidence of invasive diagnoses and revascularizations with CT, these differences have subsequently leveled off.Given these differences between CTA and functional studies, geographical differences are likely to play a role in the SCOT-HEART and PROMISE studies. In addition to the SCOT-HEART study, CTA is used in addition to a functional test, most often a treadmill stress test. Probably the confirmatory role of the functional test played a role in avoiding invasive angiography. Another factor contributing to the higher frequency of invasive diagnosis after CT scan in the PROMISE study is that it was conducted nearly a decade ago when there were no clear clinical guidelines for patient behaviour based on CT scan results.

Conclusion

CTA is being used more and more worldwide. Its high sensitivity and negative and positive predictive accuracy compared to conventional angiography make it a methodology with great diagnostic value and opportunities to influence clinical behaviour and improve prognosis in patients with chest pain. Expanding the possibilities of the methodology, including functional studies in conventional CT, helps to conduct an anonymous and functional examination in the course of tomography and comprehensive analysis of the benefits of possible revascularization and improve prevention strategies in each patient.

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