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Medium-term effects of CZT-SPECT — based treatment of coronary artery disease. Hitherto experience in the use of perfusion assessment on semiconductor gamma camera in the context of angiographic findings.

Ocena średnioterminowych efektów leczenia choroby wieńcowej w oparciu o CZT-SPECT. Dotychczasowe doświadczenia z użycia gammakamery półprzewodnikowej w ocenie perfuzji w kontekście wyników koronarografii.

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Abstract

Introduction. CZT-SPECT (cadmium-zinc telluride single photon emission tomography) is a novel upgrade of myocardial perfusion scintigraphy. This study aimed to assess the means and effects of treatment of chronic coronary syndrome in patients who have undergone CZT-SPECT and ICA (invasive coronary angiography). Secondly, the authors investigated the phenomenon of multi-focal ischaemia and defined values of perfusion defects for the prediction of revascularization and past myocardial infarction.

Materials and methods. Of 820 consecutive patients tested with CZT-SPECT, 62 with ICA performed within 90 days were chosen. Their symptoms were assessed during hospitalization and after a year in phone call interview. The occurrence of major adverse cardiac events was evaluated. Patient characteristics, data from scintigraphy, ICA and follow-up were subjected to statistical processing.

Results. CZT-SPECT was performed before ICA in 79% of cases. Less often it evaluated residual stenosis. One complication was reported. The intensity of angina and coronary stenosis burden rose with the extent of induced ischaemia. 63% of patients were qualified for revascularization. 80% of patients experienced alleviation of symptoms on follow-up. Five had major adverse events. It was found that the best cut-off of induced ischaemia for revascularization was 14% (AUC 0,798) and 8% (AUC 0,644) of fixed perfusion defect for past myocardial infarction. Multi-focal ischaemia showed bound with false positives, higher values of perfusion defect to start invasive treatment, lower left ventricle ejection fraction and coronary artery bypass-graft history. Fixed perfusion defect predicted no symptom improvement and was associated with lower ejection fraction. In false positive cases left bundle branch block and muscle bridges were frequent.

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Conclusions. CZT-SPECT is safe and contributes to lowering the number of ICAs. SPECT-based treatment effect after a year was satisfying. Multi-focal ischaemia and false positive perfusion tests likely had an impact on a higher-than--expected threshold for revascularization. Most of the false positive scintigraphies are explainable. The advantages of CZT-SPECT will ensure a rise in its role in the future.

Keywords: coronary artery disease, CZT-SPECT, invasive coronary angiography, multi-focal ischaemia, revascularization

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Introduction

Myocardial perfusion imaging (MPI) assessed in single photon emission tomography (SPECT) is a non-invasive imaging modality evaluating functional status in coronary artery disease (CAD). Involving it in clinical decision-making in patients undergoing invasive coronary artery angiography (ICA) is an optimal approach in chronic coronary syndrome. CZT (cadmium-zinc telluride) cardiac scintigraphy is still a rather new technology which is being introduced to every-day practice. This retrospective observational study depicts CZT-SPECT-guided treatment effects in the context of ICA findings. The secondary aim was to investigate multi-focal ischaemia and define cut-off values of perfusion defects for the prediction of revascularization and past infarction.

Methods

The study reviewed 820 consecutive patients who undergone MPI in the Department of Nuclear Medicine of Central Clinical Hospital of Medical University of Lodz between 01.06.2018 a 31.03.2021. Testing has been performed on Discovery NM530c (*General Electric Company, Boston, Massachusetts, USA*) semiconductor gamma camera. The radiotracer being used in the two-day stress-rest protocol was ^{99m}Tc sestamibi. Results were provided as percentages of fixed (FPD) and stress-induced perfusion defect (IPD), which were summed within types if the findings consisted of more than one region. Patients with ICA performed within the range of 90 days from MPI applied. Analysis included 62 patients, who have been assessed in Canadian Cardiac Society (CCS) score during hospitalization for ICA and after follow-up. One year follow-up included defining the type of treatment (OMT — optimal medical therapy, PCI —percutaneous coronary intervention, CABG — coronary artery bypass graft) and incidence of MACE (major adverse cardiac events) defined as death of any cause, fatal myocardial infarction, ST-elevation myocardial infarction (STEMI), non-ST-elevation myocardial infarction (N-STEMI), unstable angina (UA), early reintervention. Follow-up data have been obtained through phone call interviews, hospital data system records and healthcare insurance provider data. Patient characteristics were derived from the hospital database. The study complied with the Declaration of Helsinki.

Statistical analyses were performed with EasyMedStat ver. 3.27 (*www.easymedstat.com; Neuilly-Sur-Seine; France*) and DATAtab (*datatab.net, Graz, Austria*) online statistic software. Continuous variables were evaluated for the Gaussian distribution of the data with the Shapiro-Wilk test and presented as mean ± standard deviation or median and interquartile range (IQR). Categorical variables are presented as frequencies. For three-group comparisons, a one-way ANOVA test for multiple pair-wise comparisons was used for continuous variables, and the Pearson Chi--square test or Fisher exact test was used as appropriate for categorical variables. The strength of the association between categorical variables was given as odds ratio (OR). The equality of variance was checked by Levene's test. Two--group comparisons were performed with the Student's t-test or Welch t-test. In the case of variables showing no normal distribution, non-parametric tests were used: the Kruskal-Wallis test (three-group comparison) and the Mann–Whitney U test (two-group comparison). The alpha risk was set to 5% ($\alpha = 0.05$). For the analysis of correlations between continuous variables, the Spearman rank test was applied. For defining cut-off values Receiver Operating Characteristics were constructed.

Results

The main study results are summarized in Figure 1. The study population was 65.61 ± 8.49 years old consisting of 48 men and 14 women (tab. 1). One case was lost to follow-up. During SPECT patients underwent 22 pharmacological and 40 exertion stress tests with no statistically significant difference in both types of perfusion defects among these modalities (tab. 2). Pharmacological tests were performed predominantly using dipyridamole. Two of them used regadenosone and one — dobutamine. One adverse effect was reported: the patient in the dobutamine protocol had a pathological hypotonic drug reaction treated with adrenaline which resulted in a moderate troponin increase. In this case, ICA revealed muscle bridging on the left anterior descending artery (LAD), with haemodynamic

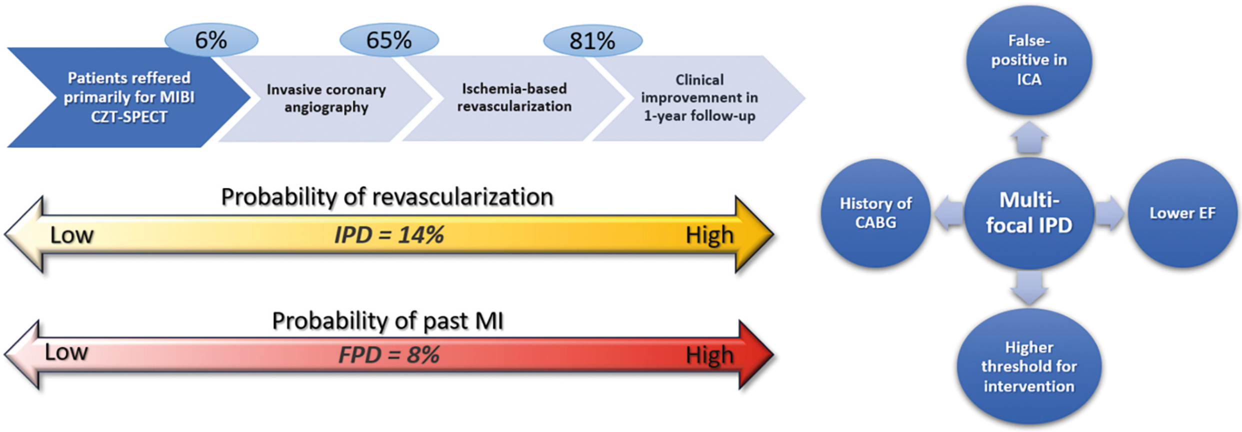

Figure 1. Main study outcomes summarization. EF — left ventricle ejection fraction; FPD — fixed perfusion defect; IPD — induced perfusion defect; MIBI CZT-SPECT — Methoxyisobutylisonitrile cadmium-zinc telluride single photon emission tomography

Table 1. Characteristics of the study group

Age (Mean ± SD)	65.61 ± 8.49
Sex (n, %)	
Men	48, 77.42%
Women	14, 22.58%
Body mass index [kg/m^2] (Mean ± SD)	27.71 ± 3.01
Ejection fraction (n, %)	
≥ 50%	43, 72.88%
41–49%	8, 13.56%
≤ 40%	8, 13.56%
Baseline CCS class (n, %)	
1	2, 5.26%
2	4, 10.53%
3	23, 60.53%
4	9, 23.68%
Follow-up CCS class (n, %)	
0	20, 58.82%
1	9, 26.47%
2	0
3	2, 5.88%
4	3, 8.82%
Diabetes mellitus (n, %)	
Yes	24, 38.71%
No	38, 61.29%
History of myocardial infarction (n, %)	
Yes	29, 46.77%
No	33, 53.23%
Smoking (n, %)	
Current	11, 17.74%
Former	22, 35.48%
Never	29, 46.77%
Intra-ventricular conduction disorders	
(n, %)	6, 9.84%
LBBB	1, 1.64%
RBBB	5, 8.2%
Other (LAFB, LPFB, RBBB+LPFB)	49, 80.33%
No conduction disorders	

History of revascularization (n, %)	
Percutaneous coronary intervention	18, 29.51%
Coronary artery bypass graft	12, 19.67%
Never	31, 50.82%
Type of stress test (n, %)	
Exertion	40, 64.52%
Pharmacological	22, 35.48%
Induced perfusion defect (n, %)	
0–5%	6, 9,68%
5–10%	12, 19.35%
≥ 10%	44, 70.97%
Fixed perfusion defect (n, %)	
0–5%	22, 37.29%
5–10%	13, 22.03%
≤ 10%	24, 40.68%
Perfusion defects configuration (n, %)	
induced-only	16, 25.81%
fixed-only	4, 6.45%
both	42. 67.74%
Type of induced perfusion defect (n, %)	
Single	45, 78.95%
Multi-focal	12, 21.05%
Myocardial perfusion test order (n, %)	
Before invasive coronary angiography	49, 79.03%
After invasive coronary angiography	13, 20.97%
Gensini score (Mean ± SD)	37.04 ± 35.11
Indications (n, %)	
Typical angina	31, 50.0%
Other symptoms (eg. dyspnoea, fatigue)	29, 46.77%
Other procedures	2, 3.23%
Number of ≥ 50% stenotic arteries in main coronary regions (n, %)	
0	12, 19.35%
1	15, 24.19%
2	17, 27.42%
3	18, 29.03%

CCS — Canadian Cardiac Society; LBBB — left bundle branch block; RBBB — right bundle branch block; LAFB — left anterior fascicular block; LPFB — left posterior fascicular block

Table 2. Perfusion defects according to patient characteristics

Variable	FPD N = 59	IPD N = 62
Sex		
Men	7.0% (IQR 11.0) Range: (0.0; 36.0) N = 45	10.0% (IQR 10.0) Range: (0.0 ; 40.0) N = 48
Women	6.0% (IQR 10.0) Range: (0.0; 30.0) N = 14	14.0% (IQR 8.75) Range: (0.0 ; 25.0) N = 14
	p = 0.52	p = 0.421
Type of stress		
Exertion	7.5% (IQR 10.0) Range: (0.0; 36.0) N = 38	10.0% (IQR 8.25) Range: (0.0; 40.0) N = 40
Pharmacological	5.0% (IQR 9.0) Range: (0.0; 25.0) N = 21	12.5% (IQR 8.0) Range: (0.0; 35.0) N = 22
	p = 0.828	p = 0.264
Myocardial perfusion test order		
Pre-ICA	5.0% (IQR 10.0) Range: (0.0; 36.0) N = 46	12.0% (IQR 8.0) Range: (5.0; 40.0) N = 49
Post-ICA	12.0% (IQR 15.0) Range: (0.0; 30.0) N = 13	5.0% (IQR 12.0) Range: (0.0; 20.0) N = 13
	p = 0.021	p < 0.001
Type of IPD		
Single	6.0% (IQR 10.0) Range: (0.0; 36.0) N = 42	10.0% (IQR 8.0) Range: (3.0; 40.0) N = 45
Multi-focal	6.0% (IQR 5.75) Range: (0.0; 30.0) N = 12	17.0% (IQR 6.5) Range: (10.0; 30.0) N = 12
	p = 0.849	p = 0.045
History of CABG		
No	7.0% (IQR 10.0) Range: (0.0; 36.0) N = 49	10.0% (IQR 8.0) Range: (0.0; 40.0) N = 51
Yes	6.5% (IQR 5.0) Range: (0.0; 30.0) N = 10	17.0% (IQR 8.0) Range: (0.0; 22.0) N = 11
	p = 0.644	p = 0.225
History of any revascularization		
No	7.0% (IQR 10.0) Range: (0.0; 36.0) N = 29	12.0% (IQR 8.0) Range: (0.0; 30.0) N = 31
Yes	5.0% (IQR 8.0) Range: (0.0; 30.0) N = 29	12.0% (IQR 9.5) Range: (0.0; 40.0) N = 30
	p = 0.981	p = 0.805
History of smoking		
No	10.0% (IQR 10.25) Range: (0.0; 30.0) N = 28	10.0% (IQR 8.0) Range: (0.0; 40.0) N = 29
Yes	5.0% (IQR 9.0) Range: (0.0; 36.0) N = 31	14.0% (IQR 10.0) Range: (0.0; 30.0) N = 33
	p = 0.611	p = 0.122
Diabetes mellitus		
No	8.0% (IQR 11.25) Range: (0.0; 36.0) N = 36	12.0% (IQR 10.25) Range: (0.0; 30.0) N = 38
Yes	5.0% (IQR 10.0) Range: (0.0; 20.0) N = 23	10.0% (IQR 10.0) Range: (0.0; 40.0) N = 24
	p = 0.324	p = 0.571
Left bundle branch block		
No	5.0% (IQR 10.0) Range: (0.0; 36.0) N = 53	11.0% (IQR 10.25) Range: (0.0; 40.0) N = 56
Yes	9.0% (IQR 2.75) Range: (0.0; 15.0) N = 6	14.0% (IQR 5.75) Range: (5.0; 20.0) N = 6
	p = 0.549	p = 0.59
Symptoms		
Typical angina	5.0% (IQR 10.0) Range: (0.0; 30.0) N = 29	15.0% (IQR 10.0) Range: (5.0; 35.0) N = 31
Others	7.0% (IQR 15.0) Range: (0.0; 36.0) N = 30	8.0% (IQR 7.0) Range: (0.0; 40.0) N = 31
	p = 0.45	p < 0.001

History of myocardial infarction		
No	4.0% (IQR 9.5) Range: (0.0; 20.0) N = 30	10.0% (IQR 8.0) Range: (0.0; 40.0) N = 33
Yes	10.0% (IQR 10.0) Range: (0.0; 36.0) N = 29	12.0% (IQR 11.0) Range: (0.0; 30.0) N = 29
	p = 0.005	p = 0.904
ICA confirmation (50% stenosis)		
True positive	5.0% (IQR 10.0) Range: (0.0; 36.0) N = 34	15.0% (IQR 8.0) Range: (10.0; 40.0) N = 37
False positive	10.0% (IQR 4.0) Range: (0.0; 20.0) N = 7	12.0% (IQR 2.5) Range: (10.0; 15.0) N = 7
	p = 0.117	p = 0.037
Ejection fraction	(ρ = -0.27; r^2 = 0.144; p = 0.044)	(ρ = -0.066; r^2 = 0.002; p = 0.619)
Body mass index	(ρ = -0.0079; r^2 < 0.001; p = 0.953)	(ρ = 0.0049; r^2 = 0.009; p = 0.97)
Gensini score	(ρ = 0.031; r^2 = 0.021; p = 0.818)	(ρ = 0.36; r^2 = 0.191; p = 0.004)

CABG — coronary artery bypass graft; FPD — fixed perfusion defect; ICA — invasive coronary angiography; IPD — induced perfusion defect

significance confirmed with fractional flow reserve (FFR). SPECT was more frequently used in pre-ICA than post-ICA assessment (49 vs. 13). Overall mean FPD was 8.069% ± 8.574 and IPD was 12.934% ± 7.930. There was no significant correlation between FPD and IPD in a single patient (ρ = –0.2; r^2 = 0.015; p = 0.133). 71% (44 of 62) of results included severe ischaemia defined as ≥ 10% IPD following European Society of Cardiology Guidelines for the diagnosis and management of chronic coronary syndromes [1].

Population characteristics

The majority of the diagnostics were due to the patient's symptoms and two of them were conducted in the course of preparation for other procedures (implantable cardioverter-defibrillator and valvular repair). Significant IPD was present in 68.75% of men and 78.57% of women cases. Patients who had SPECT preceding ICA were divided into subgroups regarding ≥ 10% IPD status. No statistically important differences in pre-test characteristics were found (tab. 3). In all cohort analyses (tab. 2) IPD showed a significant bound with occurrence of typical angina. A poor negative correlation was found between EF and FPD which was significantly higher in patients with prior myocardial infarction (MI) and a value of ≥ 8% was the best predictor (fig. 2). Patients with multi-focal IPD (described as two or more perfusion defects) irrespectively of its summed size had more often history of CABG (OR = 5.71 ; CI [1.3 ; 25.03]; p = 0.026) and lower EF (median 45% (IQR 19.5) vs. 58% (IQR 8.0); p = 0.008) compared with single IPD.

ICA findings

The prevalence of false positive scintigraphy using a 10% threshold in IPD and 70% stenosis of epicardial coronary artery in ICA in vessels not supported by bypasses was 23% (10 of 44). Using a 50% threshold of stenosis to exclude "grey-zone" narrowings decreases false positives to 16% (7 of 44). It is noteworthy, that 4 of the false positives using a 70% stenosis threshold had either slow flow phenomenon (TIMI Coronary Grade Flow = 2) or muscle bridging. Considering these results as true positives and combining them with a 50% threshold gives 11.4% of false positives (5 of 44; the precision of 88.6%). Among these patients 3 had left bundle branch block (LBBB) with septal ischaemia, one had Q waves in electrocardiogram and one had patent bypasses with occluded native arteries. Median Gensini Score, which reflects total coronary stenosis burden was 29.5 (IQR 57.25) for IPD ≥ 10% vs. 20 (IQR 30.0) for IPD < 10% (p = 0,169) with low, statistically important positive correlation with IPD (tab. 2). Both FPD and IPD didn't vary significantly regarding number of stenotic (≥ 50%) main coronary arteries but IPD had rising tendency (fig. 3). In post-ICA patients FPD was larger than in pre-ICA (tab. 2). Gensini score generally followed this trend but difference was not statistically significant: median 25.0 (IQR 59.0) for pre-ICA and 32.0 (IQR 18.0) for post-ICA (p = 0.585). Multi-focal ischaemia, LBBB and no prior revascularisation were associated with false positives (< 50% stenosis) (tab. 4). True positives had significantly higher IPD than false positives (tab. 2).

Treatment methods

The decision on therapy was made with both ICA and SPECT results available. SPECT was almost exclusively the only functional technique applied (one patient had FFR). 65% of pre-ICA and 38% of post-ICA SPECT patients were revascularized. In all population, 39 of 62 cases (63%) were qualified for revascularization: 72% (31 of 43) patients with IPD ≥ 10% and 42% (8 of 19) patients with IPD < 10%. IPD showed statistically significant differences regarding used treatment methods (p < 0.001). Pairwise

Table 3. Patient characteristics distribution in groups with severe and non-severe ischaemia

Variable	IPD ≥ 10% N = 40	IPD < 10% N = 9	p-Value
Age	66.08 (± 8.79) 95% CI: [63.26; 68.89] Range: (40.0; 81.0) N = 40	65.33 (± 3.81) 95% CI: [62.41; 68.26] Range: (61.0; 73.0) N = 9	0.696
Sex			> 0.999
Men	31 (77.5%)	7 (77.78%)	
Women	9 (22.5%)	2 (22.22%)	
	N = 40	N = 9	
Body mass index	27.73 (± 3.11) 95% CI: [26.72; 28.73] Range: (20.93; 33.31) N = 39	27.66 (± 2.9) 95% CI: [25.44; 29.89] Range: (22.99; 32.81) N = 9	0.956
Ejection fraction	56.0 (IQR 14.0) Range: (24.0; 67.0) N = 39	58.0 (IQR 5.0) Range: (43.0; 62.0) N = 9	0.596
History of smoking			0.289
no	18 (45.0%)	6 (66.67%)	
yes	22 (55.0%)	3 (33.33%)	
	N = 40	N = 9	
Diabetes mellitus			0.72
no	23 (57.5%)	6 (66.67%)	
yes	17 (42.5%)	3 (33.33%)	
	N = 40	N = 9	
History of myocardial infarction			0.72
no	23 (57.5%)	6 (66.67%)	
yes	17 (42.5%)	3 (33.33%)	
	N = 40	N = 9	
Bundle branch block			> 0.999
no	33 (82.5%)	8 (88.89%)	
yes	7 (17.5%)	1 (11.11%)	
	N = 40	N = 9	
Baseline CCS class (typical angina)			0.394
1 & 2	12 (31.58%)	3 (50.0%)	
3 & 4	26 (68.42%)	3 (50.0%)	
	N = 38	N = 6	
History of coronary artery bypass graft			0.173
no	30 (75.0%)	9 (100.0%)	
yes	10 (25.0%)	0 (0.0%)	
	N = 40	N = 9	
History of revascularization			0.159
no	20 (50.0%)	7 (77.78%)	
yes	20 (50.0%)	2 (22.22%)	
	N = 40	N = 9	

CCS — Canadian Cardiac Society; IPD — induced perfusion defect

analyses revealed differences in IPD for OMT vs. CABG (p = 0.002) and PCI vs. OMT (p = 0.009) but not for PCI vs. CABG (p = 0,4) (fig. 4). In 7 cases of 28 who underwent PCI it was performed on chronic total occlusion (CTO). Two OMT decisions in ≥ 10% IPD group resulted from the complexity of stenoses. There was no CABG in a group with IPD < 10%. Among 50–70% stenoses only 2 of 32 narrowings have been revascularized. 67.74% of patients with typical angina and 51.61% of patients with other indications (e.g. dyspnoea, fatigue) were qualified for revascularisation (OR = 0.51; CI [0.18; 1.42]; p = 0.3). Patients with multi-focal ischaemia had revascularization at higher values of

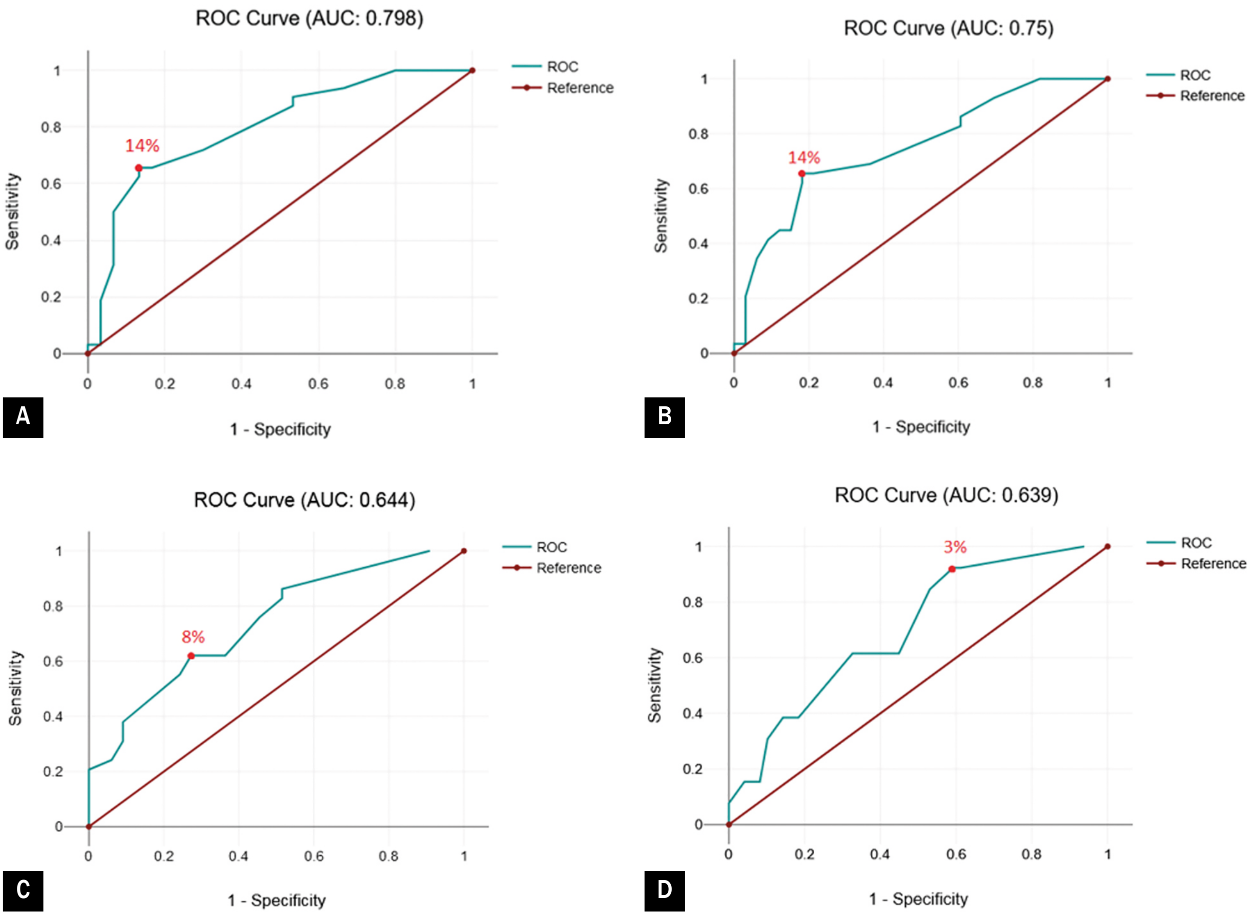

Figure 2. Receiver operating characteristics for identification of: **A.** qualification for revascularisation according to IPD (sensitivity of 66% and specificity of 87%); **B.** "improvement" on follow-up according to IPD (sensitivity 65%, specificity 82%); **C.** history of MI according to FPD (sensitivity 62%, specificity 73%); **D.** "no improvement" on follow-up according to FPD (sensitivity 92%, specificity 49%)

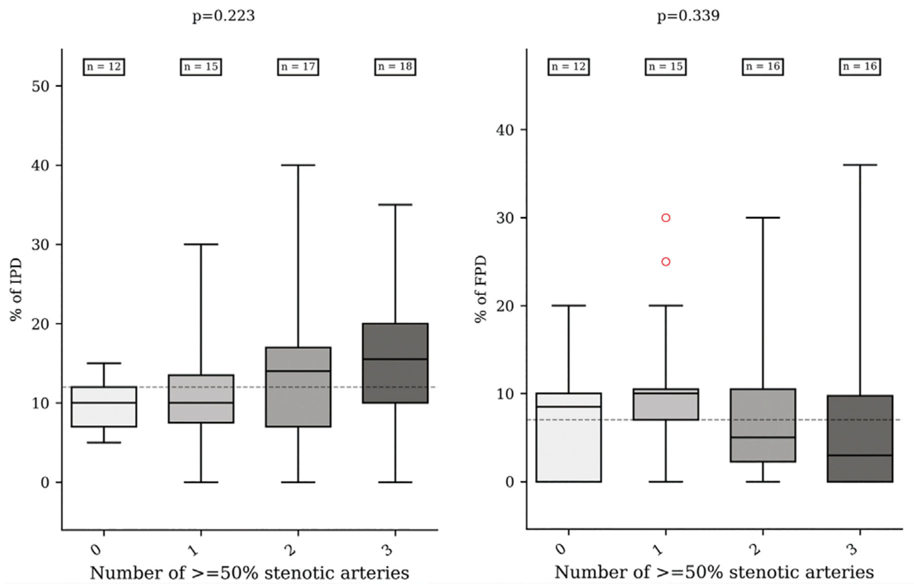

Figure 3. Distribution of perfusion defects according to number of stenotic coronary arteries. Respectively: 9.42% (SD 3.23), 11.67% (SD 7.83) 13.06% (SD 9.85) 15.5% (SD 8.35) for IPD and 8.5% (IQR 10.0), 10.0% (IQR 3.5) 5.0% (IQR 8.25) 3.0% (IQR 9.75) for FPD

Table 4. Comparison of characteristics in groups of true positive and false positive SPECT

Variable	True positive (50%) N = 37	False positive (50%) N = 7	p-Value
Age	66.05 (± 9.16) 95% CI: [63.0; 69.11] Range: (40.0; 81.0) N = 37	65.43 (± 6.9) 95% CI: [59.05; 71.81] Range: (55.0; 74.0) N = 7	0.865
Sex			0.341
Man	29 (78.38%)	4 (57.14%)	
Woman	8 (21.62%) N = 37	3 (42.86%) N = 7	
Body mass index	28.06 (± 2.91) 95% CI: [27.08; 29.04] Range: (23.15 ; 33.9) N = 36	26.68 (± 4.45) 95% CI: [22.56; 30.8] Range: (20.93; 33.31) N = 7	0.3
Type of stress test			0.682
Pharmacological	16 (43.24%)	2 (28.57%)	
Exertion	21 (56.76%) N = 37	5 (71.43%) N = 7	
Perfusion defect configuration			0.653
IPD+FPD	26 (70.27%)	6 (85.71%)	
solely IPD	11 (29.73%) N = 37	1 (14.29%) N = 7	
Myocardial perfusion test order			> 0.999
before coronarography	33 (89.19%)	7 (100.0%)	
after coronarography	4 (10.81%) N = 37	0 (0.0%) N = 7	
Type of IPD			0.011
Single	30 (81.08%)	2 (28.57%)	
Multi-focal	7 (18.92%) N = 37	5 (71.43%) N = 7	
History of coronary artery bypass graf			>0.999
No	28 (75.68%)	6 (85.71%)	
Yes	9 (24.32%) N = 37	1 (14.29%) N = 7	
History of revascularization			0.095
No	16 (43.24%)	6 (85.71%)	
Yes	21 (56.76%) N = 37	1 (14.29%) N = 7	
History of smoking			0.443
No	15 (40.54%)	4 (57.14%)	
Yes	22 (59.46%) N = 37	3 (42.86%) N = 7	
Diabetes mellitus			0.689
No	22 (59.46%)	5 (71.43%)	
Yes	15 (40.54%) N = 37	2 (28.57%) N = 7	
Ejection fraction	53.64 (± 10.77) Range: (24.0; 67.0) N = 36	48.57 (± 12.18) Range: (30.0; 65.0) N = 7	0.248
History of myocardial infarction			0.428
No	19 (51.35%)	5 (71.43%)	
Yes	18 (48.65%) N = 37	2 (28.57%) N = 7	

Intra-ventricular conduction disorders			0.005
LBBB	2 (5.41%)	3 (42.86%)	
other conduction disorders	4 (10.81%)	2 (28.57%)	
no conduction disorders	31 (83.78%)	2 (28.57%)	
	N = 37	N = 7	
Symptoms			0.675
typical angina	25 (67.57%)	4 (57.14%)	
other	12 (32.43%)	3 (42.86%)	
	N = 37	N = 7	
Baseline CCS class (typical angina)			0.202
1	1 (4.0%)	1 (16.67%)	
2	3 (12.0%)	1 (16.67%)	
3	17 (68.0%)	2 (33.33%)	
4	4 (16.0%)	2 (33.33%)	
	N = 25	N = 6	

CCS — Canadian Cardiac Society; FPD – fixed perfusion defect; IPD — induced perfusion defect; LBBB — left bundle branch block

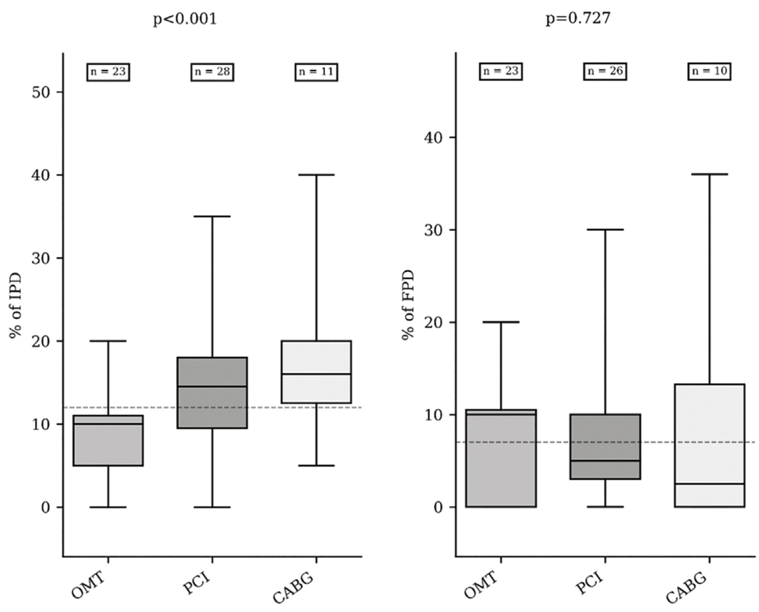

Figure 4. Distribution of perfusion defects according to type of treatment. Respectively: 8.17% (SD 5.2) 14.46% (SD 7.92) 17.82% (SD 9.29) for IPD and 10.0% (IQR 10.5) 5.0% (IQR 7.0) 2.5% (IQR 13.25) for FPD

IPD than with single-spot: median values were respectively 18.0% (IQR 2.5) and 14.0% (IQR 9.0), (p = 0.031). A value of 14% IPD was the best cut-off for predicting the decision of any revascularization (fig. 2). This threshold was valid also among true positives only (≥ 50%).

Clinical outcome and MACE

Follow-up assessment showed persistent alleviation of symptoms regardless of their type (typical and atypical) in 43 of 54 patients who met the criteria of no MACE, complete follow-up and chronic coronary syndrome as the primary indication for diagnostics. In the typical angina group, IPD generally followed the CCS class (fig. 5). and its average change was -2 on follow-up. 10 patients experiencing atypical angina or referred to diagnostic due to other planned procedures were excluded from the CCS assessment. Five patients in the analysed population had MACE (1 death, 1 NSTEMI, 1 UA, 1 subsequent early reintervention and 1 patient had 3 combined: UA, early reintervention and death). Both deaths occurred due to non-cardiac-related reasons (COVID-19). All MACE patients excluding non-cardiac death undergone PCI. Survival with subjective recovery from any type of symptoms was considered as "improvement" (distribution: CABG 91%, PCI 77%, OMT 73%) and no recovery or incidence of MACE (excluding non-cardiac death) was

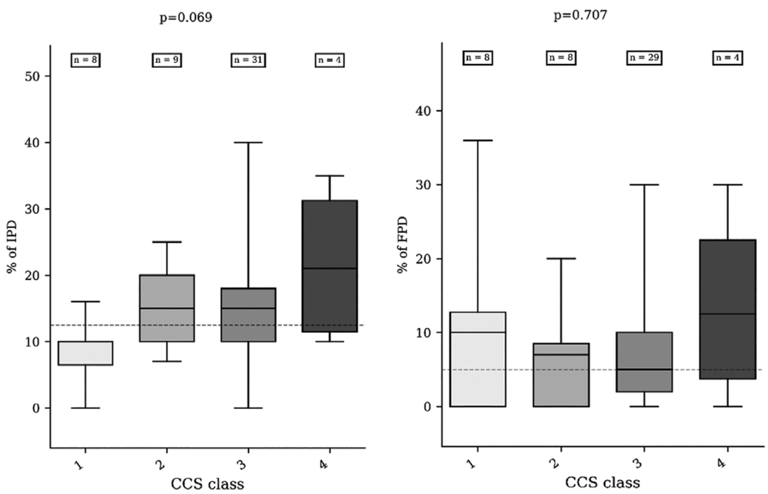

Figure 5. Distribution of perfusion defects according to severity of CAD symptoms. Respectively: 10.0% (IQR 3.5) 15.0% (IQR 10.0), 15.0% (IQR 8.0), 21.0% (IQR 19.75) for IPD and 10.0% (IQR 12.75), 7.0% (IQR 8.5), 5.0% (IQR 8.0), 12.5% (IQR 18.75) for FPD

considered as "no improvement". Generally, improvement was achieved slightly more frequently within higher values of IPD in invasive treatment (OR 1.11) and lower values of IPD in conservative treatment (OR 0.88). These tendencies were not statistically important. The difference in IPD among different clinical outcomes in the revascularized group was close to statistical importance (p = 0.069). The best cut-off of IPD predicting a good effect of revascularisation was 14% (fig. 2). Patients with false positive SPECT vs. true positive SPECT (regarding 10% of IPD and 70% stenosis) less frequently experienced improvement after a year (all have been qualified for conservative treatment) (OR = 0.18 ; CI[0.042 ; 0.81] ; p = 0.03). This group would have a 50% chance of symptom reduction without MACE compared to 84% in true positives. Patients with < 50% stenosis and positive MPI have a 57% chance of symptom alleviation on OMT. Median values of FPD were respectively 7% (IQR 10.0) in patients with improvement and 10% (IQR 15.0) in patients without improvement (p = 0.079). The value of FPD ≥ 3% best predicted no improvement in any type of treatment (fig.2).

Discussion

Modern heart-centric SPECT is a promising technology in cardiology. Semiconductor gamma cameras with multiple pinhole collimation are characterized by better spatial resolution, higher count sensitivity, lower doses of radioactivity and shorter time of acquisition compared to used hitherto general-purpose Anger cameras [2, 3]. These features contribute to better quality of images and accuracy of perfusion tests [4]. However, their disadvantage from the perspective of medical services suppliers is the inability to perform diagnostics of other organs. From the perspective of nuclear medicine specialists and technicians, placement of a patient's heart in the very centre of the camera's acquisition zone may be challenging and therefore cause artefacts [5]. It is reported, that for BMI ≥ 40 as well as women with very large breasts image quality on CZT-SPECT is non-diagnostic because of positioning difficulties and attenuation correction problems [6]. Another drawback is that this method is not suitable for very obese patients simply because of the size of the gantry. This issue does not occur in Anger cameras or D-SPECT type of CZT-SPECT. Heart placement problems do not occur in non-CZT cameras because of non-focused acquisition. In the study hospital cut-off value for disqualification from CZT-SPECT is BMI above 35.

The general prevalence of CAD-related problems after CZT-SPECT–based treatment was low and the one-year effect was satisfying. MPI acted well as a "gatekeeper" for invasive procedures (6% of patients initially referred for SPECT received ICA). Both pre-ICA and post-ICA use contributed to the reduction of redundant PCI's. A low number of "grey-zone" revascularisations in the present study comes from the fact that the majority of patients with pre-ICA SPECT had other, more severe narrowings and there was no second post-intervention SPECT performed to assess the severity of residual stenosis. Post-ICA SPECT was used mainly in patients without prior MPI with CTO and severe multi-vessel disease (MVD) (only two post-ICA patients had single-vessel disease). Therefore, the population with post-ICA tests had more advanced CAD, which caused clinical doubts.

A consensual value of 10% of IPD constituting an indication for ICA was originally derived from a study analysing which value of IPD survival was better for interventional treatment than medical therapy [7]. The present analysis suggests that with anatomical information taken into consideration, real-life decisions on intervention are made at higher values with a cut-off of 14% and interventions at these values of ischaemia showed the best treatment effect. Despite a remarkably smaller group and time of follow-up than the aforementioned study, the general treatment effect began to show an expected similar tendency of being better for invasive treatment in higher values of IPD and better for conservative treatment in lower values of IPD. The impact of FPD on the worse effect of treatment of CAD in the study cohort corresponds with previous studies [8].

Current ESC guidelines do not specify if 10% of the IPD threshold refers to single-spot ischaemia or a sum of many. Relation of multi-focal ischaemia to EF and post-CABG status possibly reflects a worse state of heart perfusion compared to equivalent single-spot ischaemia. Moreover, there seems to be some connection between multi-focal IPD and no qualification for revascularization. This may result from lack of one stenosis which is responsible for such type of ischaemia. It could be taken into consideration when analysing SPECT tests but this issue needs further investigation.

The present study shows, that most cases of false positive SPECT verified in ICA are explainable. LBBB have a known relationship with false positive septal ischaemia. This is due to mechanical dyssynchrony, compression of perforators and relative lateral wall hyperperfusion [9]. Patients without LBBB or muscle bridging are likely to have a coronary microvascular disease [10]. Because in case of muscle-bridging or microvascular disease, ICA brings important data for diagnosis (systolic vessel deflection, contrast slow-flow, index of microvascular resistance) it should not be considered redundant. This could not be said about LBBB. From the present observations, most false positive SPECT patients will experience subjective symptoms of recovery within a year of OMT. Similar BMI in false positive and true positive groups supports previous observations that CZT-SPECT operated by experienced personnel has good performance in obese patients [11].

In the present cohort, 18% of patients with angiographic MVD had negative IPD tests. It is reported that the CZT-SPECT gamma camera has fewer false negative results in the presence of MVD with "balanced ischaemia" compared to classic Anger cameras [12]. This situation globally and equally decreased coronary perfusion causes a lack of reference to define hypoperfusion. Owing to its fast acquisition, CZT-SPECT can record the first pass of radiotracer and therefore calculate absolute myocardial blood flow (MBF). This ability could bypass the aforementioned problem. The authors believe that utilisation of MBF in MVD patients in the context of invasive functional assessment is a very promising field of investigation. Secondly, the clinical approach to the issue of multi-focal ischaemia also encourages further exploration. Lastly, an important direction of future research is hybrid CZT-SPECT/angio-CT imaging, which has the potential to provide comprehensive information about coronary circulation in a single session becoming a diagnostic breakthrough.

Facing vast numbers of patients suspected of CAD in the ageing population, cath labs act as a bottleneck for diagnosis. Avoiding excessive invasive coronary diagnostics when not necessary brings safety benefits for patients. The use of SPECT-MPI will ensure the selection of patients with a high probability of intervention. Also in extensive CAD, SPECT is a useful tool in qualification for revascularization of CTO taking into account its ability to assess the viability of post-stenotic area. Techniques performed during PCI on CTO are being constantly improved. Orbital atherectomy is a good example [13]. Therefore, introducing modern PCI methods will likely contribute to the rise of the role of SPECT. It may substitute unavailable perfusion tests in positron emission tomography and unsafe dobutamine stress echocardiography. Further spreading of the CZT-SPECT technique fits into a general change of paradigm in chronic coronary syndrome from lesion-centric to ischaemia-centric [14]. Thus, performing diagnostic ICA in chronic coronary syndrome or before cardiac operations, cardioverter implantation or organ transplantation is likely to be reduced. Besides all of the above, savings for the medical care system should not be omitted.

Study limitations

It was a single-centre study. The study assessed only patients referred to ICA so there was no OMT without ICA. Analysed population was relatively small. Some patients had MPI after ICA (with or without PCI) while others had primary MPI. With one exception there was no FFR confirmation of haemodynamic significance of narrowings.

Conclusions

The utilisation of CZT-SPECT in decision-making in CAD presents great incremental value for outpatient clinicists and physicians performing ICA serving as a qualification tool for both ICA and revascularisation. SPECT-based therapy of coronary stenoses, independent of its type, gives good medium-term effects. Despite being a functional stress technique, it is characterised by high safety. Real-life decisions tend to promote invasive treatment at a higher-than-expected threshold of IPD (14%) which may be connected with false positive results and multi-focal ischaemia. The role of the latter needs further investigation. 8% of FPD best-predicted history of MI. LBBB is the most frequent reason for false positives. Still, about 1 in 10 patients with positive SPECT will receive needless ICA. Nevertheless, it is reasonable to further incorporate this technique in medical centres with a considerable number of cardiac patients.

Article information

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Author contribution
MP — writing of the manuscript, acquisition of medical data, conducting the study, statistical analysis; MB — qualification of patients for radioisotope diagnostics, acquisition of scintigraphy data; DK — writing the manuscript; KW — statistical analysis; MK — statistical analysis; JD — concept author

Ethic statement
Due to the nature of the study (retrospective, observational) the consent of the bioethics committee was not required.

Conflict of interest
The authors declare no conflict of interest.

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None

Streszczenie

Wstęp. CZT-SPECT (cadmium-zinc telluride single photon emission tomography) to nowoczesna technika stanowiąca ulepszenie scyntygrafii perfuzyjnej mięśnia sercowego. W niniejszej pracy postanowiliśmy ocenić sposoby i efekty leczenia przewlekłego zespołu wieńcowego opartego na tej technice zweryfikowanej w koronarografii. Jako cel drugorzędny chcieliśmy zbadać zjawisko wieloogniskowego niedokrwienia oraz ustanowić punkty odcięcia dla ubytków perfuzji przewidujące kwalifikację do leczenia inwazyjnego i przebyty zawał.

Materiał i metody. Spośród 820 pacjentów przebadanych na gammakamerze CZT wybrano 62, którzy w okresie 90 dni mieli wykonaną koronarografię. Oceniono nasilenie zgłaszanych objawów podczas hospitalizacji oraz po roku w wywiadzie telefonicznym. Oceniono również występowanie zdarzeń niepożądanych w tym czasie. Wynik scyntygrafii, koronarografii oraz główne charakterystyki pacjentów i dane z wywiadu telefonicznego poddano obróbce statystycznej.

Wyniki. CZT-SPECT w 79% przypadków był wykonywany przed koronarografią a rzadziej do oceny rezydualnych zwężeń. W jednym przypadku badanie było powikłane. Wraz z nasileniem miażdżycy i intensywności objawów rosła wielkość indukowanego ubytku perfuzji. Po roku u 80% pacjentów utrzymywała się redukcja objawów. 63% pacjentów było zakwalifikowanych do rewaskularyzacji. U pięciu wystąpiły zdarzenia niepożądane. Najlepszym progiem przewidującym rewaskularyzację było 14% (AUC 0,798) indukowanego niedokrwienia oraz 8% (AUC 0,644) utrwalonego niedokrwienia dla przebytego zawału. Wieloogniskowe niedokrwienie było związane z wynikami fałszywie dodatnimi, wyższymi wartościami indukowanego ubytku perfuzji przy kwalifikacji do rewaskularyzacji, niższą frakcją wyrzutową oraz wywiadem pomostowania aortalno-wieńcowego. Utrwalony ubytek perfuzji był związany z gorszym efektem leczenia i niższą frakcją wyrzutową. Wśród wyników fałszywie dodatnich częsty był blok lewej odnogi pęczka Hisa i mostki mięśniowe.

Wnioski. CZT-SPECT jest bezpiecznym sposobem obrazowania, który przyczynia się do spadku ilości diagnostyki inwazyjnej. Efekty leczenia oparte na koronarografii i scyntygrafii są satysfakcjonujące. Wieloogniskowe niedokrwienie i obecność wyników fałszywie dodatnich miały najprawdopodobniej wpływ na ustanowienie wyższego niż przewidywany progu kwalifikującego do rewaskularyzacji. Większość wyników fałszywie-dodatnich w scyntygrafii jest wytłumaczalna. Zalety CZT-SPECT zapewnią wzrost znaczenia tej metody w przyszłości.

Słowa kluczowe: choroba wieńcowa, CZT-SPECT, koronarografia, wieloogniskowe niedokrwienie, rewaskularyzacja

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