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ARTYKUŁ ORYGINALNY / *ORIGINAL ARTICLE*

Diagnostic performance of myocardial perfusion single-photon emission computed tomography with attenuation correction

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Abstract

Background: Myocardial perfusion single-photon emission computed tomography (SPECT) is one of the basic tools used for the purpose of diagnosis of coronary artery disease (CAD), prognosis of its unfavourable consequences, and evaluation of therapy effectiveness. However, its efficacy is compromised by a relatively low specificity of detection of perfusion defects, which is attributed to attenuation of gamma rays inside the patient's body, causing artefacts erroneously taken for perfusion defects. It is expected that attenuation correction (AC) could eliminate such artefacts.

Aim: To evaluate whether visual, semi-quantitative analysis of attenuation-corrected myocardial perfusion imaging provides an advantage over a non-corrected study.

Methods: A retrospective study applying AC was performed in 107 patients who had coronary angiography within three months. Patients underwent a stress/rest Tc-99m methoxyisobutylisonitrile (MIBI, POLATOM) double day SPECT/CT myocardial perfusion imaging. Images were analysed by two experienced nuclear medicine specialists (a consensus) applying a visual semiquantitative method. Coronary angiography findings were used as a reference for the analysis of diagnostic performance of myocardial perfusion study protocols.

Results: AC increased the specificity of detection of CAD in the whole group of patients from 63% to 86% ($p = 0.0005$), with a slight reduction in sensitivity (from 83% to 79%). The improved specificity was also noted in subgroups of male and female patients. Accuracy in the whole group of patients increased from 71% to 83% ($p = 0.01$). AC improved the specificity and accuracy of the method in the detection of perfusion defects in the right coronary artery (RCA) area from 73% to 88% ($p = 0.005$) and from 74% to 83% ($p = 0.04$), respectively, and the accuracy of the method in the left anterior descending (LAD) artery area from 79% to 87% ($p = 0.043$). It also reduced the number of ambiguous results of the study.

Conclusions: AC improved the diagnostic performance of myocardial perfusion study in the detection of CAD and identification of critically stenosed LAD and RCA vessels, with enhanced comfort of study interpretation.

Key words: myocardial perfusion imaging, attenuation correction, diagnostic efficacy, 99mTc-MIBI SPECT

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INTRODUCTION

Myocardial perfusion single-photon emission computed tomography (SPECT) is one of the basic tools used for the diagnosis of coronary artery disease (CAD), prognosis of its unfavourable consequences, and evaluation of therapy effectiveness. However, its efficacy is compromised by a relatively

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low specificity of detection of perfusion defects, which is attributed to attenuation of gamma rays inside the patient's body, causing artefacts erroneously taken for perfusion defects. These artefacts can be partly corrected for by gated study acquisition, which, by visualisation of regional myocardial contractility, differentiates between post-infarction scars and real artefacts. However, it is expected that a direct attenuation correction (AC) method, using a map of attenuation coefficients of the patient's thorax, acquired from a transmission study, should be more efficient in elimination of attenuation artefacts. Initially, those transmission images were acquired with the use of radionuclide sources; nowadays, X-ray tomography, a modality available in hybrid SPECT/CT cameras, is applied for this purpose. Nevertheless, although several decades have already passed since the first trials using AC methods in clinical applications of myocardial perfusion imaging have been performed, the usefulness of AC in routine imaging is still debated. This results mostly from diverse results of studies applying this correction. As well as studies demonstrating a significant improvement in diagnostic efficacy after AC [1–5], communications on its proper effects only in parts of patients with lack of improvement or even deterioration of diagnostic efficacy in the remaining ones can also be found [6–10]. The present publication is intended to add a point to this debate by determining whether visual, semi-quantitative analysis of AC myocardial perfusion imaging provides an advantage over a non-corrected study.

METHODS

A retrospective analysis was performed on 107 patients with known or suspected CAD, without clinical history, electrocardiographic or echocardiographic signs of a previous myocardial infarction, or any other factors affecting myocardial perfusion, such as cardiomyopathy, severe aortic valve disease, or left bundle branch block, referred for stress-rest myocardial perfusion SPECT in the years 2010–2014. All patients underwent coronary angiography less than three months before or after myocardial perfusion SPECT. The study group consisted of 107 patients (mean age: 62 years, body mass index: 29, echocardiographic ejection fraction: 61%), 65 males and 42 females. The whole studied group was divided into subgroups of males and females. The clinical and demographic characteristics of patients are presented in Table 1. The study was approved by the Medical University Bioethics Committee.

Table 1. Characteristics of patients

Parameter	Number
Number of patients	107
Males	65
Females	42
Mean age	62 ± 8
Mean BMI	29 ± 4
Hypertension	85
Diabetes mellitus	32
Smokers (past and present)	62
Stress study:	
Exercise	82
Pharmacological	25
Number of patients after PCI	29

BMI — body mass index; PCI — percutaneous coronary intervention

Study protocol

Patients underwent stress/rest double day myocardial perfusion imaging. In 82 (77%) patients an exercise stress test according to Bruce protocol was performed, and the remaining patients had a dipyridamole infusion (0.56–0.84 mg/kg in 4 min). Beta-blockers, nitrates, calcium channel blockers, and trimetazidine were discontinued 48 h before the stress study. Radiopharmaceutical — Tc-99m methoxyisobutylisonitryle (MIBI), at an activity of 11 MBq per kilogram of body mass, was administered intravenously at peak stress or 3–6 min after dipyridamole infusion. After administration of radiopharmaceutical the patients ate a fatty meal to accelerate hepatobiliary clearance of the tracer. Stress study acquisition was started 45 min, and rest study 1 h, after administration of radiopharmaceutical. Studies were performed with a hybrid Infinia Hawkeye (GE) camera equipped with high-resolution collimators. The study protocol consisted of the acquisition of 60 projections in a 64 × 64 matrix (zoom 1.28×). After completion of the emission study a low-dose CT study of the thorax was conducted (140 KV, 2.5 mA) in order to obtain a map of attenuation coefficients. SPECT studies were reconstructed twice, using an iterative OSEM reconstruction method (two iterations, ten subsets), with and without AC. Every time an OSEM reconstruction with AC was applied, the alignment of emission and transmission slices was visually checked. In case of misalignment CT slices were manually shifted making use of an ACQC tool, and after a proper alignment was achieved a repeat reconstruction was performed.

Image analysis

Reconstructed slices were analysed by two experienced nuclear medicine specialists (a consensus) applying a visual semiquantitative method. The method was based on a standard assignment of myocardium to three coronary arteries (left anterior descending [LAD], circumflex [Cx], and right coronary arteries [RCA]) in a way recommended by the American Heart Association [11]. Additionally, all slices in two perpendicular planes (sagittal and coronal) were also inspected according to the areas of coronary blood supply. Perfusion of three arteries was scored with the use of a 0 to 4 numerical scale, as follows: 0 — definitely normal, 1 — probably normal, 2 — equivocal, 3 — probably abnormal, and 4 — definitely

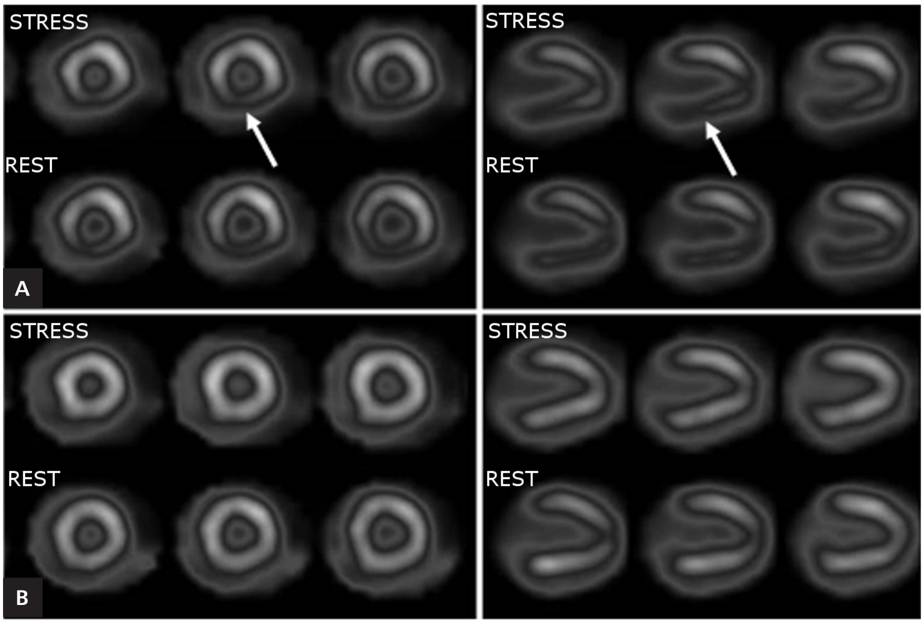

Figure 1. A study of a patient with normal coronary vessels, reconstructed without (**A**) and with (**B**) attenuation correction (AC). Arrows show inferior wall artefacts caused by attenuation of gamma radiation. AC resolved those artefacts

abnormal. When the data were dichotomised to the presence or absence of CAD, an evaluation of either definitely normal or probably normal was used to reflect scintigraphic absence of the disease. In case of presence of the disease patients were assigned the score of the most abnormal uptake in one of three coronary arteries.

The method was applied to AC as well as non-corrected images. Interpreters were informed only of the patient's sex and whether AC was applied during study reconstruction.

Coronary angiography

Invasive contrast coronary angiography was performed according to standard percutaneous techniques, with each arterial segment visualised in at least two perpendicular planes. Angiograms were analysed by experienced angiographers unaware of SPECT imaging findings. Significant CAD was defined as > 70% luminal diameter narrowing by visual inspection in at least one of the three coronary arteries (LAD, Cx, and RCA) and > 50% in the left main coronary artery. Coronary angiography findings were subsequently used as a reference for the analysis of diagnostic performance of myocardial perfusion study protocols.

Statistical analysis

Statistical analysis was performed with the statistical package Statistica 10.0. The significance of differences between scores obtained without AC and after its application was assessed with a paired Wilcoxon signed rank test. Receiver operating characteristic (ROC) curves were generated by shifting discrimination thresholds over the entire range of scores. Areas under ROC curves (AUC) were accepted as measures of ability of the method to discriminate between patients with negative and positive results of coronary angiography. Significance of differences between indices of diagnostic efficacy (sensitivity, specificity, and accuracy) obtained without and with AC was assessed with McNemar's test for paired proportions. Dependency of scores obtained without and with AC and differences in proportions of scores were tested with χ^2 independence test (with Yate's correction for continuity). Statistical significance was achieved when $p \leq 0.05$.

RESULTS

Coronary angiography

Coronary angiography revealed no critical stenosis in 65 patients and in the remaining 42: critical stenosis of one (28 patients), two (11 patients), and three (3 patients) coronary arteries.

Myocardial perfusion imaging

An example of myocardial perfusion study reconstructed without and with AC is presented in Figure 1.

Scores assigned to artery areas after application of AC were lower than without its application (median value fell from 2 to 1, $p = 0.00002$).

An increase, although non-significant, of AUC calculated for AC images in comparison with non-corrected ones in the whole group of patients was noted (0.81 vs. 0.85). This effect can be seen in Figure 2.

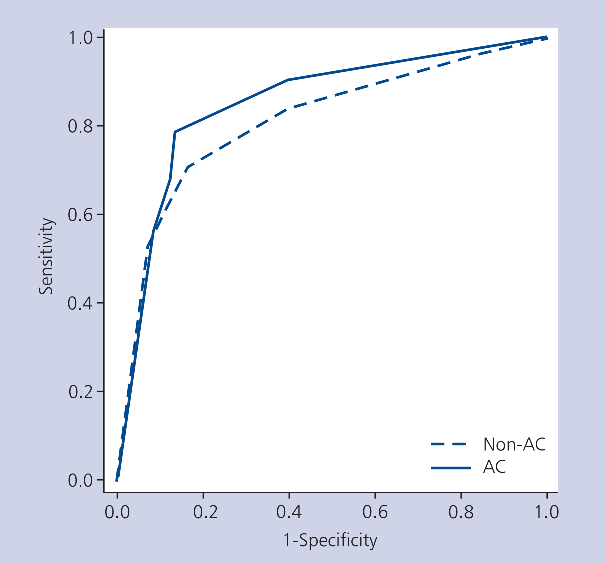

Figure 2. Receiver operating characteristic (ROC) curves obtained for the whole group of patients without (non-AC) and with (AC) attenuation correction. Areas under ROC curves (AUC) increased from 0.81 (confidence interval 0.72–0.90) to 0.85 (0.77–0.93)

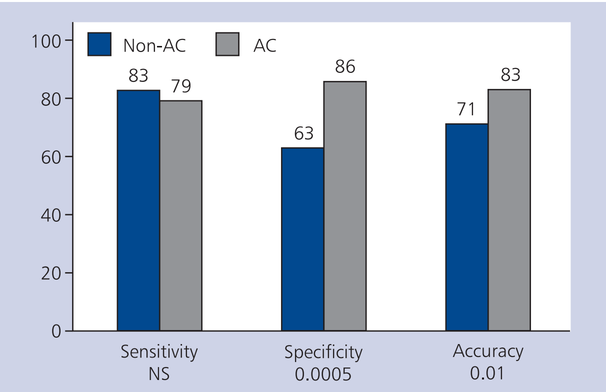

Figure 3. Diagnostic indices of myocardial perfusion study (as percentage) without (non-AC) and with (AC) attenuation correction in the whole study group (n = 107). Significance levels are specified below graphs; NS — non-significant

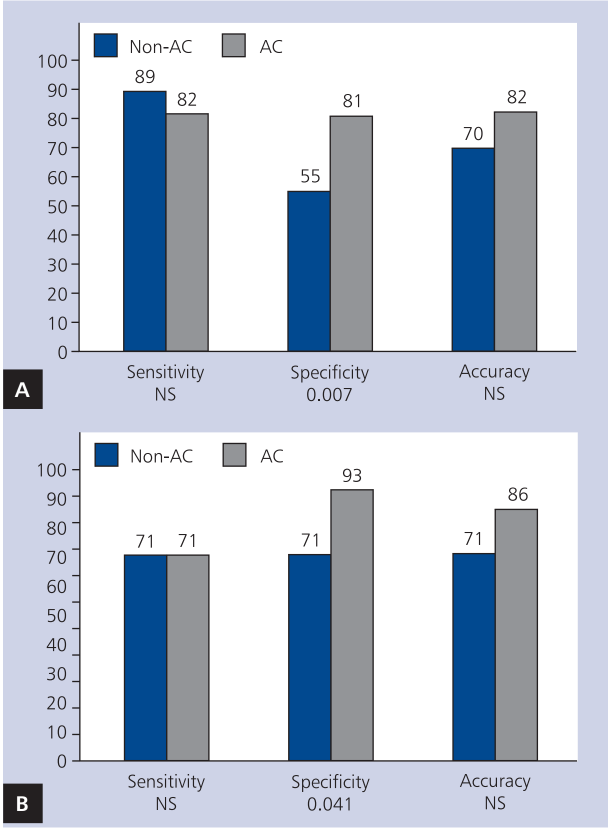

Figure 4. Diagnostic indices of myocardial perfusion study (as percentage) without (non-AC) and with (AC) attenuation correction in male and female patients. Significance levels are specified below graphs; NS — non-significant; **A**. Males (n = 65); **B**. Females (n = 42)

Figures 3 and 4 present the effect of AC of images on the diagnostic efficacy of myocardial perfusion imaging in detection of CAD. This correction statistically significantly (p = 0.0005) increased the suboptimal specificity of the method in the whole group of patients, from 63% to 86%, with slight, non-significant reduction of sensitivity of the method (from 83% to 79%). The improvement of specificity was also noted in subgroups of male (p = 0.007) and female (p = 0.041) patients. The accuracy of the method was also improved in the analysis of the entire group of patients, from 71% to 83% (p = 0.01).

In Table 2 the effect of AC on the detection of critically stenosed coronary arteries is presented. In case of LAD territory the sensitivity and specificity were improved, although both non-significantly, the former in the subgroup of males (p = 0.13) from 50% to 75%, and the latter in the subgroup of females (p = 0.07) from 76% to 91%. In effect, the accuracy of the method in detection of perfusion defects in LAD blood supply area was improved statistically significantly from 79% to 87% (p = 0.043). In the case of Cx artery without AC, three out of six stenosed vessels were detected, whereas after application of AC this number was reduced to one. As for RCA territory, specificity was considerably improved in the subgroup of males, from 58% to 83% (p = 0.0006), resulting in an increase of this index of diagnostic efficacy in the whole group of patients, from 73% to 88% (p = 0.005). In effect, the accuracy of the method was also improved in the subgroup of males, from 66% to 80% (p = 0.045), and in all studied patients from 74% to 83% (p = 0.04).

In summary, the effect of application of AC was that the number of all correctly detected stenosed vessels was slightly reduced from 35/57 (61%) to 33/57 (58%), but significant

Table 2. Effect of attenuation correction (AC) on detection of critically stenosed vessels

		Without AC	With AC	P
Left anterior descending artery	Sensitivity:			
	All	13/24 = 54%	17/24 = 71%	NS
	Male	8/16 = 50%	12/16 = 75%	NS
	Female	5/8 = 63%	5/8 = 63%	NS
	Specificity:			
	All	72/83 = 87%	76/83 = 92%	NS
	Male	46/49 = 94%	45/49 = 92%	NS
	Female	26/34 = 76%	31/34 = 91%	NS
	Accuracy	85/107 = 79%	93/107 = 87%	0.043
Circumflex artery	Sensitivity	3/6 = 50%	1/6 = 17%	NS
	Specificity	97/101 = 96%	97/101 = 96%	NS
	Accuracy	100/107 = 93%	98/107 = 92%	NS
Right coronary artery	Sensitivity:			
	All	18/23 = 78%	15/23 = 65%	NS
	Male	15/17 = 88%	12/17 = 71%	NS
	Female	3/6 = 50%	3/6 = 50%	NS
	Specificity:			
	All	61/84 = 73%	74/84 = 88%	0.005
	Male	28/48 = 58%	40/48 = 83%	0.0006
	Female	33/36 = 92%	34/36 = 94%	NS
	Accuracy:			
	All	79/107 = 74%	89/107 = 83%	0.04
	Male	43/65 = 66%	52/65 = 80%	0.045
	Female	36/42 = 85%	37/42 = 88%	NS

improvement of specificity and accuracy in detection of critical stenoses in RCA area of blood supply and also an improvement of accuracy in detection of critically stenosed LAD arteries were achieved.

Attenuation correction, as shown in Table 3, mostly affected scores assigned to images of patients without critically stenosed vessels ($p = 0.00002$), with minimal changes in patients with stenosed arteries. This correction statistically significantly increased the number of patients assigned a score of 0 (definitely normal) in a subgroup of patients without critically stenosed vessels, from 15 to 39 ($p = 0.0004$) and also statistically significantly reduced numbers of ambiguous results of one (probably normal) — from 25 to 17 ($p = 0.02$) and two (equivocal) — from 14 to one ($p = 0.001$).

Table 3. Effect of attenuation correction (AC) on patient scores in subgroups of patients with positive and negative results of coronary angiography (n = 107 patients)

Score	Number of patient scores			
	Positive result of coronary angiography		Negative result of coronary angiography	
	Without AC	With AC	Without AC	With AC
0	3	3	15	39
1	4	5	25	17
2	5	4	14	1
3	7	8	6	3
4	23	22	5	5

DISCUSSION

During four decades of clinical trials applying AC in myocardial perfusion SPECT abundant literature relating to this topic has been published. The results presented in those articles are quite diverse. Some of them report evident improvement of diagnostic efficacy after AC, with a statistically significant improvement of specificity, accuracy, and normalcy rate, as well as improvement of localisation of stenosed vessels [1], others report improvement of sensitivity and specificity without differences in normalcy rate, or improvement of only normalcy rate without changes of sensitivity and specificity (those differences were attributed to individual tendencies of interpreters using visual, semi-quantitative methods of image inspection) [4], improvement of normalcy rate without reduction of sensitivity [8], and improvement of specificity in detection of perfusion defects in inferior wall with reduction of specificity in anterior wall [9]. Several publications can also be found reporting improved specificity, but at the cost of reduced sensitivity of detection of CAD [9, 12].

This inconsistency of results should be attributed to the high complexity of the method and several sources of variability: the geometry, the kind of transmission source, the software applied for tomographic reconstruction of a study, the structure of the studied group of patients (percentage of patients with negative results of coronary angiography or low probability of CAD), and the methods applied for interpretation of studies. Moreover, many authors use only AC [1, 4, 9, 10, 12] while others also apply scatter correction [2, 5, 13, 14] and resolution recovery [13]. In this multitude of factors affecting results of clinical studies it is very difficult to determine the real effect of AC on diagnostic efficacy of detection of CAD. Nonetheless, in the results of those studies some trends can be observed. Attenuation correction usually improves normalcy rate or specificity of the study (the latter holds true only if the percentage of patients with negative results of coronary angiography in the whole studied material is high enough) [2, 10, 15]. Improvement of accuracy can usually be observed as an effect of enhanced specificity, without [5] or with marked decline of sensitivity of the study [9, 12]. This results mostly from a reduction of number of perfusion defects observed in the inferior wall of the myocardium, which unfortunately affects not only false positive, but also some part of true positive defects. In theory, a scatter correction (elimination of gamma rays originating from structures lying close to the myocardium but registered erroneously inside its region) could improve the situation, but no unquestionable results including this correction positively affecting study sensitivity have been found as yet [5, 13].

In the present study evaluation of myocardial perfusion imaging after AC improved discrimination capacity between patients with positive and negative results of coronary angiography (increase of areas under ROC curves), although this effect did not reach statistical significance. To our knowledge, from all of the available literature dealing with this problem Ficaro et al. [1] were the only authors who obtained statistically significant improvement of discrimination between patients with and without stenosed vessels after application of AC (statistically significant increase of area under ROC curve). In the present work joint use of AC with visual, semiquantitative evaluation of areas of three coronary arteries improved statistically significantly the specificity and accuracy of the method, as compared with non-corrected studies, from 63% and 71% to 86% and 83%, respectively, with a slight reduction of sensitivity of the method (from 83% to 79%). Moreover, improvement of specificity was attained also in subgroups of males and females. This can be attributed to the presence of tissues attenuating radiation, such as diaphragm and breasts, causing artefacts imitating perfusion defects.

The results of this study, unlike the findings presented in a publication by Wolak et al. [16], evidently indicate the feasibility of AC in the subgroup of female patients. Wolak et al. [16] demonstrated a lack of improvement of a diagnostic efficacy of attenuation corrected vs. non-corrected myocardial perfusion imaging in female patients. This disagreement may result from the different methods applied for evaluation of both studies. Wolak et al. [16] used a quantitative method based on an objective criterion: a precise cutoff between positive and negative study results, whereas in the case of a visual method equivocal images appear inevitably, which are resolved by AC leading to improvement of the diagnostic efficacy of the method.

The low (71%) sensitivity of the method in the detection of CAD in females was probably a consequence of the low number female patients with critically stenosed vessels (13 patients).

A strong effect of study group characteristics and subjectivity factor affecting visual image interpretation can be observed in the study by Sharma et al. [12], who used the same equipment, software, and method for image interpretation as the authors of the work herein. In their publication a significant reduction of sensitivity with improvement of specificity as a result of application of AC was obtained by two interpreters, resulting in a drop in accuracy but increase in normalcy rate. This reduction of accuracy might have been an effect of the small percentage (below 30%) of patients with negative results of coronary angiography, whereas the evident reduction of sensitivity might have been caused by a subjective tendency of study interpreters toward a high specificity rather than sensitivity, as well as the higher percentage of patients with critically stenosed vessels in the studied material.

The authors of the present work decided to eliminate patients who underwent myocardial infarction from the studied material to avoid ambiguities resulting from confusion of defects caused by postinfarction scars and critically stenosed vessels. To our knowledge this is the only publication on the effect of AC on the diagnostic efficacy of myocardial perfusion imaging using a relatively large material of patients without myocardial infarction.

In the present work the effect of AC on the detection of perfusion defects in areas of coronary arteries could be observed mostly in the RCA area, where a statistically significant improvement of specificity and accuracy of the method was attained in the subgroup of male patients, at the cost of a slight reduction of sensitivity of the method. In the LAD area both sensitivity and specificity increased insignificantly, with improvement of the former noted in males, and of the latter in females. These two factors taken together formed a statistically significant increase of the accuracy of the method in the detection of critically stenosed LAD in the whole group of patients. An improved detection rate of the left anterior descending CAD was also reported by Shotwell et al. [5] Improvement of specificity the detection of stenosed LAD observed in our study indicates that AC did not introduce additional artefacts in the anterior wall of myocardium, an argument that is raised by authors against application of AC [17]. Several authors have reported such artefacts [18, 19], including recently Huang et al. [10], who observed a reduction of specificity in anterior wall as an effect of AC. Such artefacts are thought to be the effect of overcorrection of the inferior wall [18, 19], causing a relative reduction of counts in anterior wall, leading to induction of false perfusion defects.

Although coronary angiography is not an ideal reference method for myocardial perfusion imaging, it is still used by many authors as a gold standard [5, 9, 10, 12] because no better method of verification of myocardial perfusion study results is available. The prognostic value of this study, treated as a verification method, takes a long time to be determined.

A statistically significant reduction of the number of equivocal results of myocardial perfusion study should be considered an additional advantage of the AC because it improves the convenience of study interpretation.

CONCLUSIONS

The AC of myocardial perfusion study applied in the present work significantly improved the specificity and accuracy of semiquantitative myocardial perfusion assessment, as compared with a non-corrected study protocol, in the detection of CAD. Increased specificity of the method was also attained in subgroups of males and females. Identification of critically stenosed vessels was improved mostly in cases of RCA (resulting from increased specificity of the method in the area of this artery) but also of LAD artery. Attenuation correction significantly reduced the number of patients with equivocal results, improving the convenience of study interpretation.

Conflict of interest: *none declared*

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Skuteczność diagnostyczna scyntygrafii perfuzyjnej mięśnia sercowego z zastosowaniem korekty osłabiania promieniowania

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Streszczenie

Wstęp: Scyntygrafia perfuzyjna mięśnia sercowego techniką SPECT stanowi cenne narządzie diagnostyczne służące przede wszystkim wykrywaniu choroby wieńcowej (CAD), prognozowaniu jej niekorzystnych następstw oraz ocenie skuteczności terapii. Jednak skuteczność diagnostyczna tej metody wykazuje ograniczenia w postaci suboptymalnej swoistości, wynikającej z osłabiania promieniowania gamma w ciele pacjenta, co skutkuje powstawaniem artefaktów, omyłkowo branych za ubytki perfuzji. Uważa się, że zastosowanie korekty osłabiania powinno poprawić skuteczność diagnostyczną tej metody.

Cel: Celem pracy było zbadanie, czy wizualna, półilościowa metoda oceny zastosowana do scyntygramów z korekcją osłabiania promieniowania poprawia skuteczność diagnostyczną metody w wykrywaniu CAD.

Metody: Badaniem retrospektywnym objęto pacjentów, u których scyntygrafie przeprowadzono w sposób umożliwiający zastosowanie korekty osłabiania promieniowania. Badana grupa składała się ze 107 pacjentów (65 mężczyzn i 42 kobiet), u których w odstępie czasu nie dłuższym niż 3 miesiące wykonano koronarografię. Badanie perfuzji mięśnia sercowego (wysiłkowe i spoczynkowe) przeprowadzono techniką SPECT/CT, wg protokołu 2-dniowego, po podaniu radiofarmaceutyku Tc-99m-metoksyizobutylizonitrylu (MIBI, POLATOM). Obrazy oceniało dwóch doświadczonych specjalistów medycyny nuklearnej, metodą konsensusu. Wyniki koronarografii traktowano jako weryfikację wyników scyntygrafii perfuzyjnej.

Wyniki: Korekta osłabiania promieniowania poprawiła swoistość wykrywania CAD w całej grupie pacjentów, z 63% do 86% (p = 0,0005), przy nieznacznym obniżeniu czułości metody (z 83% do 79%), także w badanych podgrupach mężczyzn i kobiet. Dokładność metody wzrosła w całej grupie pacjentów z 71% do 83% (p = 0,01). Korekta osłabiania poprawiła swoistość i dokładność metody w wykrywaniu ubytków ukrwienia zlokalizowanych w prawej tętnicy wieńcowej, odpowiednio z 73% do 88% (p = 0,005) oraz z 74% do 83% (p = 0,04), a także w gałęzi przedniej zstępującej lewej tętnicy wieńcowej — z 79% do 87% (p = 0,043). Korekta ta zmniejszyła także liczbę wyników wątpliwych.

Wnioski: Zastosowanie korekty osłabiania promieniowania poprawiło skuteczność diagnostyczną scyntygrafii perfuzyjnej mięśnia sercowego techniką SPECT w wykrywaniu CAD oraz krytycznie zwężonych naczyń: prawej tętnicy wieńcowej oraz gałęzi przedniej zstępującej lewej tętnicy wieńcowej. Dzięki zmniejszeniu udziału wyników wątpliwych korekta ta poprawiła także komfort interpretacji scyntygramów.

Słowa kluczowe: scyntygrafia perfuzyjna mięśnia sercowego, korekta osłabiania promieniowania, skuteczność diagnostyczna, ^{99m}Tc-MIBI SPECT

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