Folia Cardiologica 2019
tom 14, nr 3, strony 235–241
DOI: 10.5603/FC.2019.0055

ISSN 2353–7752

Detection of ischaemia with myocardial perfusion imaging using ^{99m}Tc-MIBI SPECT in patients suspected of having, or who have, stable coronary artery disease

Diagnostyka choroby niedokrwiennej serca za pomocą scyntygrafii perfuzyjnej z użyciem izotopu ^{99m}Tc-MIBI u pacjentów chorujących lub diagnozowanych w kierunku stabilnej choroby wieńcowej

Agnieszka Stępień[1], Katarzyna Holcman[2], Przemysław Poznański[1], Mateusz Jakosz[1], Radosław Cieciak[1], Magdalena Kostkiewicz[2, 3]

[1]Students' Scientific Group Medical Imaging in Cardiology, Department of Cardiac and Vascular Diseases, Jagiellonian University Medical College, John Paul II Hospital, Krakow, Poland
[2]Department of Cardiac and Vascular Diseases, Jagiellonian University Medical College, John Paul II Hospital, Krakow, Poland
[3]Nuclear Medicine Department, John Paul II Hospital, Krakow, Poland

Agnieszka Stępień jest studentką VI roku kierunku lekarskiego *Collegium Medicum* Uniwersytetu Jagiellońskiego w Krakowie. Swoją działalność naukową wiąże z pracą w Studenckim Kole Naukowym Obrazowania Medycznego w Kardiologii działającym pod kierownictwem prof. dr hab. n. med. Magdaleny Kostkiewicz przy Klinice Chorób Serca i Naczyń Krakowskiego Szpitala Specjalistycznego im. Jana Pawła II. Zainteresowania medyczne skupia na zagadnieniach kardiologicznych. Wolny czas poświęca na podróże i sport.

Abstract

Introduction. Myocardial perfusion single-photon emission computed tomography (SPECT) is a diagnostic method using radionuclides to assess heart muscle perfusion. The aim of this study was to assess adherence to the European Society of Cardiology (ESC) guidelines in referring patients to SPECT and to evaluate the occurrence of perfusion disorders depending on the type of indication.

Material and methods. The study included 100 outpatients (45 males), of mean age 65 ± 10 years, who were referred for SPECT in the John Paul II Hospital in Kraków. According to the 2013 ESC Guidelines of stable coronary artery disease (CAD) management, indications for this study are those patients: with electrocardiogram (ECG) anomalies at rest, which prevent its accurate interpretation during stress (1st); with pacemaker (2nd); who are symptomatic with prior revascularisation (3rd); who are unable to exercise adequately during a stress test (4th); and with uncharacteristic chest pain (5th). Patients were divided into two groups according to their SPECT study result. Group 1 comprised patients with perfusion disorders, and Group 2 patients without perfusion disorders.

Address for correspondence: Agnieszka Stępień, Oddział Kliniczny Chorób Serca i Naczyń z Pododdziałem Intensywnego Nadzoru Kardiologicznego, Krakowski Szpital Specjalistyczny im. Jana Pawła II, ul. Prądnicka 80, 31–202 Kraków, Poland, e-mail: agaa.stepien@gmail.com

Results. SPECT perfusion disorders were detected in 53 patients (53%) (these patients made up Group 1). Compliant with ESC Guidelines referrals included: 8% of patients with the 1st indication, 2% with the 2nd, 24% with the 3rd, 15% with the 4th and 23% with the 5th. Apart from the aforementioned indications, referrals including 'CAD' and 'another heart arrhythmia' were noted in 32% and 7%, respectively. From all the above mentioned ESC indications for SPECT, we observed statistically significant differences in the prevalence of perfusion disorders solely in patients with the 3rd indication on their referrals (p = 0.013).

Conclusions. Overall, 72% of referrals in this study were compliant with ESC Guidelines. The most common indications for SPECT were 'CAD' and 'symptomatic patients with prior revascularisation'. Only the group of patients with the 3rd indication had statistically significantly more frequent perfusion disorders in SPECT.

Key words: SPECT, coronary artery disease, myocardial perfusion imaging

Folia Cardiologica 2019; 14, 3: 235–241

Introduction

Myocardial perfusion single photon emission computed tomography (SPECT) is a non-invasive imaging method evaluating cardiac muscle perfusion with the use of radionuclides. Since SPECT's introduction at the start of the 1990s [1, 2], its role in diagnosing ischaemic heart disease has considerably increased. An improvement in the field of coronary heart disease (CAD) invasive treatment has been observed over recent decades. This has resulted in a growing number of patients surviving acute myocardial infarction (AMI). It has also given an opportunity to implement treatment in the early stages of CAD, prior to AMI. As a result, there has been increased interest in methods of assessing myocardial perfusion disorders, as well as left ventricular function after revascularisation procedures. Such interest has led to further development of SPECT, nowadays an established diagnostic method in CAD evaluation. Currently SPECT is used for AMI risk stratification [3–6] and it guides clinicians in deciding whether a further diagnostic or therapeutic intervention should be considered [7, 8]. The experience gathered from almost 30 years of performing SPECT has helped to establish the European Society of Cardiology (ESC) Guidelines [9] for referring patients to this examination. Therefore, the purpose of our study was to assess the adherence to these guidelines in referring patients to SPECT and to evaluate the occurrence of perfusion disorders depending on the type of indication.

Material and methods

Patients

This retrospective observational study included 100 consecutive patients who were referred for a SPECT study in the John Paul II Hospital, Krakow. Data was obtained from patients' referrals and SPECT study results. Our study examined SPECT scans performed between October and December 2017.

Referrals

According to the 2013 ESC Guidelines of Stable CAD Management [9], indications for this study are:

- patients with electrocardiogram (ECG) anomalies at rest which prevent its accurate interpretation during stress;
- patients with pacemaker;
- symptomatic patients with prior revascularisation;
- patients who are unable to exercise adequately during stress test;
- patients with uncharacteristic chest pain.

SPECT protocol

All patients underwent the two-day ^{99m}Tc-sestamibi imaging protocol in accordance with the European Association of Nuclear Medicine procedural guidelines [10]. To provide the stress test, physical activity or pharmacological stressing was applied, depending on referral indications.

Exercise testing using the Bruce protocol was performed [10]. Endpoints of exercise stressing were:

- reaching 85% of predicted maximum heart rate;
- typical chest pain or equivalent (dyspnoea);
- ischaemic ECG abnormalities: diagnostic horizontal or downsloping ST depression of > 2–3 mm;
- significant ventricular or supraventricular arrhythmia on ECG;
- a progressive reproducible decrease in systolic blood pressure;
- abnormal elevation of systolic blood pressure and maximum stress (fatigue) [10].

Pharmacological testing is dedicated for patients with orthopaedic, neurological, or peripheral vascular disease and patients on beta-blocking medication, who are unable to increase their heart rate adequately by physical exercise. Two pharmacological stressors were used in our study: dipyridamole or dobutamine, adequately to patients' own contraindications. For every imaging session, 20 mCi (740 MBq) of ^{99m}Tc-methoxy isobutyl isonitrile (MIBI) was administered. All SPECT studies were acquired on a Siemens

Symbia gamma camera and were gated by ECG recording, which allowed us to calculate left ventricular ejection fraction (LVEF).

Statistical analysis

Shapiro-Wilk test was used to assess normality. The *t*-test was used for normally distributed variables, and the Mann-Whitney U test for non-normally distributed variables. Nominal variables were analysed using the Chi^2 test. In the analysis, differences were considered statistically significant for a p-value less than 0.05. Statistical analysis was performed with RStudio v. 8.5.

Results

Baseline patient characteristics are set out in Table 1. Of the 100 patients, 45 were men. The mean age was 65 years, with mean height: 166 centimetres (cm), mean weight: 81.98 kilograms (kg), and mean body mass index (BMI): 29.65 kg/m^2. In this group 46% of patients were obese, *i.e.* with a cut-off value of BMI higher than 30 kg/m^2.

To provide the stress test, 34 of the patients underwent pharmacological stressing. Among these 33 (97%) were given dipyridamole and in one (3%) patient with asthma dobutamine was administered. 66 patients underwent an exercise test. Among these, 25 (38%) reached at least 85% of the age-predicted maximum heart rate and the remaining 41 (62%) failed to do so. The most common cause of early termination of the test was patient fatigue.

For statistical analysis, we divided patients into two groups: the first group with perfusion disorders revealed in SPECT (53 patients, which we called Group 1) and the second group, without abnormalities in myocardial perfusion (47 participants, Group 2). Group 1 included 29 (54.7%) men and 24 (45.3%) women, while in Group 2 there was a predominance of females [16 men (34%), 31 women (66%), p = 0.01]. The demographic characteristics of patients depending on their perfusion disorder occurrence are set out in Table 2. There was a statistically significant difference between the groups in mean values of weight (86.21 kg vs. 77.35 kg, p = 0.006) and BMI (30.8 kg/m^2 vs. 28.5 kg/m^2, p = 0.03). Analysis of other parameters *i.e.* age and height did not demonstrate significant differences between the groups (p > 0.05).

Table 1. Baseline characteristics of all patients included in the study*

Parameter	Value
Gender: male/female	45 (45%)/55 (55%)
Mean age [years]	65 ± 10.36
Mean height [cm]	166 ± 9
Mean weight [kg]	81.98 ± 17.44
Mean BMI [kg/m^2]	29.65 ± 5.96
Overweight or obese	46 (46%)

*Variables are shown as mean values with standard deviation; BMI — body mass index

Overall in this study 72% of referrals were compliant with ESC Guidelines. Table 3 shows the distribution of indications, according to the referrals, depending on the SPECT result. In the group with perfusion disorders, three patients (5.66%) had ECG anomalies at rest, which precluded its accurate interpretation during stress (the 1st indication), one subject (1.89%) had a pacemaker (the 2nd indication), 18 participants (33.96%) were referred as symptomatic patients with prior revascularisation (the 3rd indication), seven patients (13.21%) were unable to exercise adequately during the stress test (the 4th indication), and 10 people had uncharacteristic chest pain. In comparison, the group without perfusion disorders included: five (10.64%) patients who had ECG anomalies at rest which precluded its accurate interpretation during stress, one (2.13%) with a pacemaker, six (12.77%) who were referred as symptomatic patients with prior revascularisation, eight people (17.02%) were unable to exercise adequately during the stress test, and 13 participants (27.66%) were referred with uncharacteristic chest pain. As already stated, there was a statistically significant difference between the groups only in the prevalence of the 3rd indication (p = 0.013). Apart from the aforementioned indications, compliant

Table 2. Demographic profile of patients divided into two groups according to single-photon emission computed tomography (SPECT) study result: Group 1 — patients with perfusion disorders, Group 2 — patients without perfusion disorders

Parameter	Group 1 (N = 53)	Group 2 (N = 47)	p value
Gender: male/female	29 (54.7%)/24 (45.3%)	16 (34%)/31 (66%)	0.01
Mean age [years]	65.04 ± 9.7	66.6 ± 11	0.2
Mean height [cm]	167 ± 9	165 ± 9	0.06
Mean weight [kg]	86.21 ± 17.66	77.35 ± 15.97	0.006
Mean BMI [kg/m^2]	30.8 ± 5.91	28.5 ± 5.81	0.03
Overweight/obese	25 (47%)	19 (40%)	0.14

*Variables are shown as mean values with standard deviation; BMI — body mass index

Table 3. Distribution of indications for single-photon emission computed tomography (SPECT) study according to 2013 European Society of Cardiology guidelines on the management of stable coronary artery disease. Patients divided into two groups according to SPECT study result: Group 1 — patients with perfusion disorders, Group 2 — patients without perfusion disorders

Indication for SPECT study	Group 1 (N = 53)	Group 2 (N = 47)	P value
ECG anomalies at rest which prevent its accurate interpretation during stress	3 (5.66%)	5 (10.64%)	0.36
Pacemaker	1 (1.89%)	1 (2.13%)	0.93
Symptomatic patient with prior revascularisation	18 (33.96%)	6 (12.77%)	0.013
Unable to exercise adequately during stress test	7 (13.21%)	8 (17.02%)	0.59
Non characteristic chest pain	10 (18.87%)	13 (27.66%)	0.3

ECG — electrocardiogram

with the ESC guidelines, indications including 'CAD' and 'another heart arrhythmia' were noted in this study. In the group with perfusion disorders, 14 (26.42%) patients had 'CAD' on their referrals and two (3.77%) had an 'another heart arrhythmia' indication. Group 2 had 18 (38.30%) patients referred for SPECT with 'CAD' and five (10.64%) with 'another heart arrhythmia'. Overall, there were no differences between the groups in terms of the prevalence of those indications ($p = 0.2$ for 'CAD' and $p = 0.18$ for 'another heart arrhythmia').

Patients with perfusion disorders more often had a decreased left ventricular ejection fraction (LVEF) of below 55%, as opposed to Group 2 where the figures were [29 (55%) vs. 5 (11%), $p < 0.01$].

Discussion

In our study, we observed a predominance of males in the patients with abnormal SPECT study results (54.7% in Group 1 vs. 34% in Group 2). Shaw et al. [11] examined 3,975 middle-aged patients referred for outpatient stress testing. The authors found that coronary revascularisation procedures were done more frequently in men (4.9% vs. 2%, $p = 0.03$) which is associated with the higher perfusion disturbances prevalence in this group. The majority of patients referred to SPECT in this study were women (55%). A study by Hemal et al. [12] compared the two genders and proved that women were more often referred for imaging tests than for non-imaging tests. Women also were less likely to have a positive test result, which is compatible with our results (43.6% women vs. 64.4% men, $p = 0.01$).

Obesity is an increasing concern for healthcare providers worldwide [13]. In our study, 46% of the referred patients were overweight or obese. There was a trend towards a higher prevalence of overweight and obese in participants with perfusion disturbances found in SPECT study (47% vs. 40%, $p = 0.14$). Accordingly, the group with myocardial perfusion disorders had statistically significant higher BMIs than the group without perfusion disturbances (30.8 kg/m^2 vs. 28.5 kg/m^2). This finding is concordant with the current knowledge that these are independent risk factors for numerous cardiovascular diseases including CAD [14]. There are studies currently being carried out evaluating whether hormones produced by adipose tissue could be an independent risk factor for myocardial ischaemia. In the future, these could be used in clinical practice to assess the risk of CAD [15].

In our study, the most frequently used indication in patients referred to SPECT was: 'symptomatic patient with prior revascularisation'. The number of these patients is high due to increasingly widespread use of revascularisation techniques, especially percutaneous coronary intervention (PCI). In the case of patients who have undergone PCI in the past and now present with symptoms, physicians have to consider both restenosis and the progression of CAD. Casses et al. [16] found that in a group of 10,004 patients who underwent PCI, restenosis occurred in 26.4% of them. The risk of restenosis was lower when drug-eluting stents (DES) were used compared to bare-metal stents (BMS). Additionally, second-generation DESs posed a lower risk of restenosis than first-generation DESs. Despite the progression in the field of PCI, this complication is still considered a relevant difficulty.

The problem of symptoms recurrence also concerns patients after coronary artery bypass graft (CABG) procedures. In this group, there are two main clinical problems in long term observation. The first is the progression of CAD in other arteries of coronary circulation [17]. The second is the durability of the graft. Goldman et al. reported that internal mammary artery grafts had 85% 10-year patency, while for saphenous vein grafts the 10-year patency was 61% [18].

In our study, 24 patients were referred with the abovementioned indication. Perfusion disorders were detected in 18 of them (75%). According to previous studies, the occurrence of perfusion disorders in patients after revascularisation relevantly worsens the prognosis [19]. Our study showed that 75% of symptomatic patients with prior revascularisation had perfusion disorders in SPECT. Thus, a scintigraphy result may be especially useful in this group in establishing the best therapeutic approach

and in deciding about the subsequent invasive procedure. Our findings emphasise the risk of progression of CAD in symptomatic patients after cardiac revascularisation. Early diagnosis of CAD progression may decrease the number of additional diagnostic tests and, as a result, reduce the time to appropriate treatment implementation. Furthermore, there is contraindicatory data relating to stress testing implementation, including myocardial perfusion SPECT, routinely after revascularisation procedures. The current guidelines of cardiological and nuclear medicine societies (*e.g.* ESC, European Association of Nuclear Medicine, Polish Cardiac Society) advise that the stress test not be performed after revascularisation as standard, given the fact that the usefulness of this diagnostic approach has not yet been investigated properly [8–10]. However, some data on routinely performed SPECT emphasises its potential benefits [20]. Despite the role of SPECT in the evaluation of symptomatic patients being well established, a routinely performed SPECT could bring about logistical problems for healthcare providers, due to issues such as the accessibility of the study and cost-effectiveness.

In our study, eight patients presented with ECG anomalies that meant it could not be accurately interpreted during the exercise test. Those abnormalities included an ST segment depression of 1 mm during rest ECG and left bundle branch block (LBBB). In general, patients with aforementioned ECG changes are at a higher risk of death from CAD [21]. Nonetheless, the value of myocardial perfusion SPECT might be decreased in patients with LBBB. In this group, a false positive result may be observed due to the exercise anteroseptal perfusion disorders phenomenon [22]. Three (5.66%) of our participants had perfusion disorders, and five (10.64%) had a correct SPECT study result ($p = 0.34$).

The results of the studies support the statement that myocardial perfusion SPECT is a good method of risk stratification in patients presenting with ECG anomalies that mean it cannot be accurately interpreted during an exercise test. Consequently, SPECT results are used to assess which of the patients is in need of revascularisation, and who would not benefit from this procedure [23].

Dominguez-Rodriguez et al. [24] assessed factors affecting the adequacy of indications in referring to SPECT. Their analysis showed that experience gained since the completion of cardiology training influenced the referrals' quality and the accuracy of the chosen study. Furthermore, some studies have proved that using appropriate indications for SPECT in the population with CAD is cost-effective [25].

Conclusion

Overall in this study 72% of referrals were compliant with ESC Guidelines. Apart from the aforementioned indications, referrals including 'CAD' and 'heart arrhythmia' were noted. Results from our study show that among ESC Guidelines indications for myocardial perfusion SPECT, the most common was exacerbation of symptoms in patients with prior revascularisation. Only this group of patients had statistically significantly more frequent perfusion disorders in SPECT. Overall, males and patients with a higher BMI were more prone to cardiac ischaemia. Moreover, patients with perfusion disorders in a SPECT study more often had decreased left ventricle systolic function.

Conflict(s) of interest

The authors declare that there is no conflict of interest.

Streszczenie

Wstęp. Scyntygrafia perfuzyjna mięśnia sercowego wykonywana metodą tomografii emisyjnej pojedynczego fotonu (SPECT) jest badaniem diagnostycznym wykorzystującym izotopy do oceny aktywności biologicznej mięśnia sercowego. Celem niniejszego badania była ocena przestrzegania wytycznych Europejskiego Towarzystwa Kardiologicznego (ESC) w zakresie kierowania pacjentów na badanie SPECT i oceny występowania zaburzeń ukrwienia w zależności od rodzaju wskazania.

Materiały i metody. Do badania włączono 100 pacjentów ambulatoryjnych (45 mężczyzn) w średnim wieku 65 ± 10 lat, którzy zostali skierowani na badanie scyntygrafii perfuzyjnej mięśnia sercowego do Krakowskiego Szpitala Specjalistycznego im. Jana Pawła II w Krakowie. Zgodnie z wytycznymi ESC z 2013 roku dotyczącymi postępowania w stabilnej chorobie wieńcowej (CAD) na badanie SPECT powinni być skierowani pacjenci: z zaburzeniami elektrokardiograficznymi (EKG) w spoczynku, które uniemożliwiają ich poprawną interpretację w trakcie wysiłku (1.), z rozrusznikiem serca (2.), pacjenci wykazujący objawy po wcześniejszej rewaskularyzacji (3.), którzy nie są w stanie wykonać testu wysiłkowego (4.), z nietypowymi bólami w klatce piersiowej (5.). Pacjentów podzielono na dwie grupy według wyniku badania SPECT (grupa 1. — pacjenci z zaburzeniami perfuzji, grupa 2. — pacjenci bez zaburzeń perfuzji).

Wyniki. Zaburzenia perfuzji w badaniu SPECT wykryto u 53 pacjentów (53%) (grupa 1.). Przestrzeganie wytycznych ESC dotyczących wskazań do badania scyntygraficznego zaobserwowano kolejno u: 8% pacjentów z pierwszym wskazaniem, 2% z drugim, 24% z trzecim, 15% z czwartym i 23% z piątym. Poza wymienionymi wyżej wskazaniami na skierowaniach pojawiły się również wskazania „CAD" i „inna arytmia serca" kolejno u 32% i 7% pacjentów. W odniesieniu do wszystkich wymienionych wyżej wskazań ESC dotyczących SPECT zaobserwowano statystycznie istotne różnice w zakresie częstości występowania zaburzeń perfuzji wyłącznie u pacjentów z trzecim wskazaniem na ich skierowaniach (p = 0,013).

Wnioski. Wśród skierowań na badanie scyntygraficzne mięśnia sercowego 72% było zgodnych z wytycznymi ESC z 2013 roku. Najczęściej pojawiającymi się wskazaniami były „CAD" i „objawowi pacjenci po wcześniejszej rewaskularyzacji". Tylko w grupie pacjentów z trzecim wskazaniem statystycznie istotnie częściej występowały zaburzenia perfuzji w badaniu SPECT.

Słowa kluczowe: SPECT, choroba wieńcowa, perfuzja serca, scyntygrafia perfuzyjna

Folia Cardiologica 2019; 14, 3: 235–241

References

1. Notghi A, Low CS. Myocardial perfusion scintigraphy: past, present and future. The Br J Radiol. 2011; 84(special issue 3): 229–236.
2. Sharir T, Slomka P. Dual-isotope myocardial perfusion SPECT imaging: past, present, and future. J. Nucl. Cardiol. 2018; 25(6): 2024–2028., doi: 10.1007/s12350-017-0966-0, indexed in Pubmed: 28664393.
3. Brown KA. Prognostic value of thallium-201 myocardial perfusion imaging. A diagnostic tool comes of age. Circulation. 1991; 83(2): 363–381, indexed in Pubmed: 1991361.
4. Hachamovitch R, Berman DS, Shaw LJ, et al. Incremental prognostic value of myocardial perfusion single photon emission computed tomography for the prediction of cardiac death: differential stratification for risk of cardiac death and myocardial infarction. Circulation. 1998; 97(6): 535–543, indexed in Pubmed: 9494023.
5. Stratmann HG, Williams GA, Wittry MD, et al. Exercise technetium-99m sestamibi tomography for cardiac risk stratification of patients with stable chest pain. Circulation. 1994; 89(2): 615–622, indexed in Pubmed: 8313549.
6. Iskander S, Iskandrian A. Risk assessment using single-photon emission computed tomographic technetium-99m sestamibi imaging. J Am Coll Cardiol. 1998; 32(1): 57–62, doi: 10.1016/s0735-1097(98)00177-6.
7. Hachamovitch R, Hayes SW, Friedman JD, et al. Comparison of the short-term survival benefit associated with revascularization compared with medical therapy in patients with no prior coronary artery disease undergoing stress myocardial perfusion single photon emission computed tomography. Circulation. 2003; 107(23): 2900–2907, doi: 10.1161/01.CIR.0000072790.23090.41, indexed in Pubmed: 12771008.
8. Płońska Go, Kostkiewicz M, Pasowicz M, et al. Myocardial viability imaging in ischaemic heart disease, part 2: current role of radionuclide imaging. Expert consensus statement of the Polish Clinical Forum for Cardiovascular Imaging. Kardiol Pol. 2012; 70(8): 857–865.
9. Montalescot G, Sechtem U, Achenbach S, et al. Task Force Members, ESC Committee for Practice Guidelines, Document Reviewers. 2013 ESC guidelines on the management of stable coronary artery disease: the Task Force on the management of stable coronary artery disease of the European Society of Cardiology. Eur Heart J. 2013; 34(38): 2949–3003, doi: 10.1093/eurheartj/eht296, indexed in Pubmed: 23996286.
10. Verberne HJ, Acampa W, Anagnostopoulos C, et al. European Association of Nuclear Medicine (EANM). EANM procedural guidelines for radionuclide myocardial perfusion imaging with SPECT and SPECT/CT: 2015 revision. Eur J Nucl Med Mol Imaging. 2015; 42(12): 1929–1940, doi: 10.1007/s00259-015-3139-x, indexed in Pubmed: 26290421.
11. Shaw LJ, Miller DD, Romeis JC, et al. Gender differences in the noninvasive evaluation and management of patients with suspected coronary artery disease. Ann Intern Med. 1994; 120(7): 559–566, indexed in Pubmed: 8116993.
12. Hemal K, Pagidipati NJ, Coles A, et al. Sex differences in demographics, risk factors, presentation, and noninvasive testing in stable outpatients with suspected coronary artery disease: insights from the PROMISE Trial. JACC Cardiovasc Imaging. 2016; 9(4): 337–346, doi: 10.1016/j.jcmg.2016.02.001, indexed in Pubmed: 27017234.
13. Finucane M, Stevens G, Cowan M, et al. National, regional, and global trends in body-mass index since 1980: systematic analysis of health examination surveys and epidemiological studies with 960 country-years and 9·1 million participants. The Lancet. 2011; 377(9765): 557–567, doi: 10.1016/s0140-6736(10)62037-5.
14. Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation. 1983; 67(5): 968–977, doi: 10.1161/01.cir.67.5.968.
15. Hung CS, Wu YW, Huang JY, et al. Evaluation of circulating adipokines and abdominal obesity as predictors of significant myocardial ischemia using gated single-photon emission computed tomography. PLoS One. 2014; 9(5): e97710, doi: 10.1371/journal.pone.0097710, indexed in Pubmed: 24842767.
16. Cassese S, Byrne RA, Tada T, et al. Incidence and predictors of restenosis after coronary stenting in 10 004 patients with surveillance angiography. Heart. 2014; 100(2): 153–159, doi: 10.1136/heartjnl-2013-304933, indexed in Pubmed: 24270744.
17. Weintraub W, Clements S, Crisco LT, et al. Twenty-year survival after coronary artery surgery. Circulation. 2003; 107(9): 1271–1277, doi: 10.1161/01.cir.0000053642.34528.d9.
18. Goldman S, Zadina K, Moritz T, et al. VA Cooperative Study Group #207/297/364. Long-term patency of saphenous vein and left

internal mammary artery grafts after coronary artery bypass surgery: results from a Department of Veterans Affairs Cooperative Study. J Am Coll Cardiol. 2004; 44(11): 2149–2156, doi: 10.1016/j.jacc.2004.08.064, indexed in Pubmed: 15582312.

19. Acampa W, Petretta MP, Daniele S, et al. Myocardial perfusion imaging after coronary revascularization: a clinical appraisal. Eur J Nucl Med Mol Imaging. 2013; 40(8): 1275–1282, doi: 10.1007/s00259-013-2417-8, indexed in Pubmed: 23604804.
20. Eisenberg MJ. Routine periodic stress testing in asymptomatic patients following coronary revascularization: is it worth the effort?: comment on "Exercise testing in asymptomatic patients after revascularization". Arch Intern Med. 2012; 172(11): 861–863, doi: 10.1001/archinternmed.2012.1910, indexed in Pubmed: 22905353.
21. Eriksson P, Wilhelmsen L, Rosengren A. Bundle-branch block in middle-aged men: risk of complications and death over 28 years. The Primary Prevention Study in Göteborg, Sweden. Eur Heart J. 2005; 26(21): 2300–2306, doi: 10.1093/eurheartj/ehi580, indexed in Pubmed: 16214833.
22. Lebtahi N. Left bundle branch block and coronary artery disease: accuracy of dipyridamole thallium-201 single-photon emission computed tomography in patients with exercise anteroseptal perfusion defects. J Nucl Cardiol. 1997; 4(4): 266–273, doi: 10.1016/s1071-3581(97)90103-3.
23. Ten Cate TJF, Kelder JC, Plokker HWM, et al. Patients with left bundle branch block pattern and high cardiac risk myocardial SPECT: does the current management suffice? Neth Heart J. 2013; 21(3): 118–124, doi: 10.1007/s12471-011-0174-5, indexed in Pubmed: 21695525.
24. Dominguez-Rodriguez A, Avanzas P, Abreu-Gonzalez P, et al. [Influence of the professional experience of the clinical cardiologist on the adequacy of the clinical indications of myocardial perfusion gated-SPECT]. Arch Cardiol Mex. 2018; 88(5): 386–390, doi: 10.1016/j.acmx.2017.11.001, indexed in Pubmed: 29198595.
25. Dos Santos MA, Santos MS, Tura BR, et al. Budget impact of applying appropriateness criteria for myocardial perfusion scintigraphy: the perspective of a developing country. J Nucl Cardiol. 2016; 23(5): 1160–1165, doi: 10.1007/s12350-016-0505-4, indexed in Pubmed: 27229342.