Assessment of myocardial perfusion and viability with stress Tc–99m–MIBI SPECT before surgical revascularisation. Correlation with postoperative perfusion improvement

Anna Teresińska¹, Marian Śliwiński², Bożenna Szumilak¹, Stefania Konieczna¹, Elżbieta Gosiewska-Marcinkowska¹, Zbigniew Juraszyński², Piotr Hendzel², Maria Szymańska²
¹Department of Nuclear Medicine, Institute of Cardiology, Warsaw, Poland
²First Clinic of Cardiac Surgery, Institute of Cardiology, Warsaw, Poland

BACKGROUND: The immediate result of successful revascularisation of the myocardium is the improvement of perfusion (and in patients with depressed ventricular function, functional recovery is expected as an effect of coronary flow improvement). The main goal of the work was to assess the value of myocardial stress-rest MIBI perfusion scintigraphy in predicting myocardial perfusion state measured early (< 5 months) after CABG.

MATERIAL AND METHODS: Forty-three patients (39 males, mean age 52 ± 9 years) with chronic coronary artery disease underwent prerevascularisation and postrevascularisation stress-rest Tc-99m-MIBI SPECT studies. Eighty-one percent of patients had a history of myocardial infarction, the number of stenosed main coronary arteries was 2.3 ± 0.6 per patient, and the left ventricle ejection fraction was 18–70% (mean 46 ± 14%).

Correspondence to: Anna Teresińska
Department of Nuclear Medicine, Institute of Cardiology
ul. Alpejska 42, 04-628 Warsaw, Poland
Tel. (+48 22) 8154714, fax: (+48 22) 8154003
e-mail: ANNATIK@POLBOX.COM

Preoperative perfusion defects were considered as small, medium or severe (depending upon stress uptake deficiency) and as transient or persistent (depending upon uptake improvement in rest). Changes in perfusion defects (improvement, lack of changes or deterioration) were evaluated very early after CABG (mean 31 ± 12 days) in all patients and additionally about 3 months later (mean 119 ± 17 days after CABG) in 36 patients.

RESULTS: In transient perfusion defects, the probability of early postoperative perfusion improvement was 80% (in small defects: 89%, CI₀.₉₅ = 80–94%) and was significantly higher than in small persistent defects (51%) and than in medium- and severe persistent defects (21%). In medium- and severe persistent defects, the lack of changes in perfusion was observed in 76% of defects (in severe defects: 81%, CI₀.₉₅ = 69–91%) and was significantly higher than in small persistent defects (37%), than in medium- and severe transient defects (17%), and than in small transient defects (4%). The probability of later postoperative perfusion improvement was 78% in transient perfusion defects (in small defects: 85%, CI₀.₉₅ = 74–92%) and was significantly higher than in small, medium, and severe persistent defects (28%). In medium- and severe persistent defects, the lack of changes in perfusion was observed in 71% of defects (in severe defects: 81%, CI₀.₉₅ = 66–91%) and was significantly higher than in small persistent defects (40%), and than in severe, medium, and small transient defects (11%).

CONCLUSIONS: 1. The result of preoperative stress-rest Tc–99m-MIBI SPECT myocardial perfusion study is an exact predictor of the state of perfusion measured early (< 5 months) after CABG; the postoperative regional perfusion improvement is most dependent upon reversibility and also upon severity of stress defect. 2. In small persistent defects, changes in perfu-
sion are different than in other types of defects — so they should not be considered together with transient defects (as "viable") or with persistent defects (as "nonviable"). 3. Preoperative viability assessment on the basis of Tc-99m-MIBI study performed solely in rest is unjustified: at the similar perfusion defect at rest, the presence of even minimal inducible ischaemia is associated with increased probability of perfusion improvement after CABG.

Key words: myocardial perfusion, SPECT, Tc-99m-MIBI, CABG

Introduction

A positive result of myocardial revascularisation is the effect of improvement of the myocardial blood flow, with possible consecutive improvement of regional or global function of the left ventricle (LV), and/or lowered mortality, and/or improved quality of life. Revascularisation can significantly increase perfusion and function of LV, even in patients with chronic left ventricular dysfunction — but only in the regions with preserved viability of myocytes.

Tc-99m-MIBI (2-methoxy-isobutyl-isonitrile) is a relatively new compound with proved value in the diagnosis of coronary artery disease and with clinically tested utility in myocardial viability assessment [1–4]. The efficiency of the techniques assessing myocardial perfusion and viability is usually postoperatively evaluated on the basis of function improvement, most often by echocardiography (ECHO) [5–9]. Such an approach is not accurate because of differences in techniques used pre- and post-operatively (perfusion v. function evaluation, planar views (ECHO) v. tomographic sections (SPECT) used, different doctors assessing the study) and because the improvement of LV function can depend on the time interval from operation (reperfusion stunning, prolonging for a few months after revascularisation, can take place). Postoperative control study performed in the same way as preoperative Tc-99m-MIBI SPECT study seems to be the only precise method of evaluation of the changes in perfusion caused by revascularisation. An independent, further, part of evaluation can be investigation of the functional changes caused by perfusion changes.

The main goal of this work was to assess the value of the stress-rest myocardial perfusion Tc-99m-MIBI SPECT technique in predicting the postoperative state of perfusion, measured early (< 5 months) after surgical revascularisation with the same technique. Our purpose was also to study the dynamics of perfusion changes during the first months after operation.

Material and methods

Patients

The group consisted of 43 patients (39 males, 34–69 years old, mean: 52 ± 9 years) submitted to coronary artery bypass grafting surgery (CABG) because of chronic coronary artery disease documented angiographically. Thirty-five patients (81%) had a history of previous myocardial infarctions (MI), however no patient had had an acute MI within 2 months preceding the study. One patient underwent three MI, 12 patients underwent two MI, 22 patients underwent one MI, and 8 patients were without a history of MI (mean: 1.1 ± 0.8 MI per patient). Left ventricle ejection fraction, evaluated on the basis of contrast ventriculography in 25 patients, was 0.18–0.70 (mean: 0.46 ± 0.14). Sixteen patients had significant stenosis (> 70% narrowing in luminal diameter) of three major coronary vessels, 22 patients — of two vessels, and 5 patients — of one vessel (mean: 2.3 ± 0.6 vessels disease per patient).

Surgical revascularisation

All operations were performed after sternotomy, using extracorporeal circulation. During the operation, in 18 patients (42%) there were 1–5 venous grafts implemented (mean: 3.3 ± 1.2 grafts), in 4 patients (9%) there were 1–3 arterial grafts (mean: 1.8 ± 1.0 grafts), in 21 patients (49%) there were 2–5 venous and arterial grafts (mean: 3.0 ± 0.7 grafts). Mean number of grafts per patient was 3.0 ± 1.0. All the patients had uncomplicated postoperative recovery.

Segments of the LV with perfusion defects were affiliated to territories of three major coronary vessels, according to the standard algorithm [10]. Perfusion of anterior wall, antero-septal wall and apex was connected with left anterior descending artery (7 segments), inferior and infero-septal walls — with right coronary artery (6 segments), and lateral wall — with left circumflex artery (4 segments). It was assumed that a defect (a segment) was revascularised during CABG if there was a graft implemented to the artery responsible for blood flow to the segment.

Imaging protocol

In all 43 patients, Tc-99m-MIBI stress-rest single-photon emission computed tomography (SPECT) was performed 2 times: before CABG (not earlier than 6 months before CABG, SPECT-0) and early after CABG (< 2 months, SPECT-I). In 36 patients (84%) next control study was also performed (< 5 months after CABG, SPECT-II).

Stress and rest studies were performed after separate tracer injections, on consecutive days, in a random sequence. Stress tests were performed according to a modified Bruce protocol (MAX-1 Marquette exercise system with Series 1900 treadmill). After at least 4-hours fasting, a dose of 1.11 MBq per 1 kg of body weight of Tc-99m-MIBI was injected. SPECT data acquisition commenced 60 to 120 minutes after tracer injection in rest and 45–90 minutes after injection in stress. Image sets were obtained from 64 projections over 180-degree arc beginning at 45-degree right anterior oblique and ending at 45-degree left posterior oblique projection. A low-energy high-resolution, parallel-hole collimator and a 64 × 64 matrix with no zoom were used. Processing was performed with filtered back-projection using one-dimensional Butterworth filter with a cut-off frequency of 0.4 of Nyquist frequency and the order of 7; interslice weighting 1-2-1 was applied after transverse reconstruction. Images were corrected for nonuniformity and for centre of rotation displacement. From transaxial tomograms, the short-axis, vertical long-axis, and horizontal long-axis tomograms were derived. From the short-axis slices, the BULL’S-EYE maps [10, 11] in stress and in rest were generated. SPECT imaging was done by a single-head gamma camera (ORBITER 75, Siemens) connected with MaxDELTA 2000 computer system (Siemens).

Image analysis

Perfusion assessment was performed visually on the basis of vertical long-axis tomograms, horizontal long-axis tomograms and the BULL’S-EYE maps. Perfusion was evaluated after dividing the LV into 17 segments (four segments corresponded to the anterior
wall, four to the lateral wall, four to the inferior wall, four to the septum and one to the apex). The severity of the uptake defect in stress was assessed on a 4-grade intensity scale (0 — no defect, 1 — small defect, 2 — medium defect, 3 — severe defect). According to that, all perfusion defects were divided into 6 types: small, medium, and severe persistent defects (when there was no perfusion improvement in rest in comparison to stress) and small, medium and severe transient defects (when there was perfusion improvement in rest).

In postoperative studies, perfusion improvement in a segment was described if the defect severity decreased in stress and rest, in stress only (and there was no change in rest), or in rest only (and there was no change in stress). Perfusion deterioration in a segment was described if the defect severity increased in stress and/or rest. Perfusion improvement in a patient was described when the number of segments with perfusion improvement was higher than the number of segments with perfusion deterioration (considering only the segments with preoperative perfusion defects).

Each SPECT study was assessed by three observers experienced in nuclear cardiology and the results were established by consensus. The study protocol was approved by the State Committee for Scientific Research.

Statistical analysis
All continuous variables were represented as a mean and one standard deviation. Mean values were first evaluated by F-test (p = 0.05) for variances equality and then the t-test (p = 0.05) for means with equal or non-equal variances was used to compare them. Rates of segments or rates of patients with perfusion preserved, improved or deteriorated were described as variables with binomial distribution and 95-percent confidence intervals (CI_{0.95}) were calculated for assessment of the equality of the rates.

Results

Date of studies
SPECT studies were performed in the following time schedule: SPECT-0: 3–179 (mean: 57 ± 52) days before CABG, SPECT-I: 13–62 (mean: 31 ± 12) days after CABG, SPECT-II: 87–154 (mean: 119 ± 17) days after CABG. The interval between SPECT-I and SPECT-II was 52–130 (mean: 89 ± 20) days, i.e. about three months.

Revascularisations
During the operations there were revascularised 331 of 368 (90%) segments with preoperative perfusion defects.

Results of perfusion assessment
In SPECT-0, 368 segments were diagnosed as perfusion defects (on average: 9 defects per patient): there were 119 persistent defects (35 small, 30 medium and 54 severe) and 249 transient defects (83 small, 114 medium and 52 severe). Among transient defects, there were only 5 totally reversible defects — for that reason they were not treated separately and the term “transient” concerns the group of 244 partially reversible defects (98%) and 5 (2%) totally reversible defects. Changes in perfusion in postoperative studies in relation to preoperative study in all types of defects are presented in Table 1. No significant differences in the number of segments with perfusion improvement, preservation or deterioration were found between all defects of a given type and a subgroup of corresponding revascularised defects. For that reason, in further part of the presentation, all defects of a given type (revascularised and nonrevascularised) were considered together, for the sake of better statistics.

Perfusion in SPECT-I in comparison to SPECT-0 (top of Figure 1; for details see Table 1). In all types of transient defects (small, medium or severe), the percentage of defects with perfusion improvement was similar (89%, 77% and 73%) and was significantly higher than the percentage with perfusion preservation (4%, 16% and 21%) and with perfusion deterioration. In small persistent defects, the percentage of defects with perfusion improvement was still (but insignificantly) higher than the percentage with perfusion preservation (51% v. 37%). In medium persistent defects, there was an inverse relation: the percentage of defects with perfusion improvement was significantly lower than the percentage with perfusion preservation (27% v. 67%); in severe persistent defects, the relation was similar (19% v. 81%). The percentage of defects with perfusion improvement in transient defects on average was 80% (in small transient defects: 89%, CI_{0.95} = 80–94%) and was significantly higher than in small persistent defects (51%) and than in medium and severe persistent defects altogether (21%). The percentage of defects with no changes in perfusion in medium and severe persistent defects was 76% (in severe persistent defects: 81%, CI_{0.95} = 69–91%) and was significantly higher than in small persistent (37%), than in medium and severe transient (17%) and than in small transient defects (4%). The percentage of defects with perfusion deterioration in postoperative study was similar in every type of defect (0–11%).

Perfusion in SPECT-II in comparison to SPECT-0 (bottom of Figure 1; for details see Table 1). In all types of transient defects (small, medium or severe), the percentage of defects with perfusion improvement was similar (85%, 73% and 79%) and was significantly higher than the percentage with perfusion preservation (6%, 14% and 11%) and with perfusion deterioration — like in SPECT-I. In small persistent defects, the percentage of defects with perfusion improvement was similar to the percentage with perfusion preservation (33% v. 40%); in medium persistent defects, the relation was similar (36% v. 57%). In severe persistent defects, the percentage of defects with perfusion improvement was significantly lower than the percentage with perfusion preservation (19% v. 81%) — like in SPECT-I. The percentage of defects with perfusion improvement in transient defects on average was 78% (in small transient defects: 85%, CI_{0.95} = 74–92%) and was significantly higher than in small, medium and severe persistent defects (altogether 28%). The percentage of defects with no changes in perfusion in medium and severe persistent defects was 71% (in severe persistent defects: 81%, CI_{0.95} = 66–91%) and was significantly higher than in small persistent (40%) and than in severe, medium and small transient defects (altogether 11%). The percentage of defects with perfusion deterioration in postoperative study was similar in every type of defect (0–13%) but small persistent defects, in which it was higher (27%).

Dynamics of perfusion changes between SPECT-I and SPECT-II (Figure 2; for details see Table 2). Changes in perfusion in postoperative SPECT-I in relation to later SPECT-II were calculated in 36 patients who underwent both postoperative studies in all types of defects. As previously (Tab. 1), no significant
differences in the number of segments with perfusion improvement, preservation or deterioration between all corresponding defects of a given type and a subgroup of revascularised defects of a given type were found. Similarly as before, therefore, in the further part of this presentation, all defects of a given type (revascularised and nonrevascularised) were considered, combined for the sake of better statistics. The percentage of defects with perfusion improvement, preservation or deterioration between two postoperative studies was similar in every type of defects but severe persistent defects, in which there was a significantly higher percentage of segments with perfusion preservation (90% v. 62%) and a significantly lower percentage with perfusion deterioration (2% v. 19%).

**Diagnostic concordance of the results from SPECT-I and SPECT-II.** Concordance of the postoperative results (SPECT-I and SPECT-II) in the area of the defective segment was claimed if in both studies the perfusion was better, unchanged or worse than in preoperative study (SPECT-0). Concordance for different types of defects was similar (73–97%, globally: 87%,

**Figure 1.** Graphical illustration of postoperative changes in different types of preoperative myocardial perfusion defects (95%-confidence intervals for printed values are given in Table 1). Top: changes in very early postoperative study (SPECT-I), bottom: changes in later postoperative study (SPECT-II) — in comparison to preoperative state.

**Figure 2.** Graphical illustration of dynamics in perfusion changes between very early postoperative study and later study (95%-confidence intervals for printed values are given in Table 2).
The history of small persistent defects. In those defects, changes in perfusion were different than in other types of defects. In the early postoperative study, they presented perfusion improvement less often (51%) than transient defects (80%) but more often than other persistent defects (21%). On the other hand, they presented no changes in perfusion less often (37%) than other persistent defects.
defects (76%) but more often than transient defects (13%). It was the only group of defects in which the percentage of defects with the same perfusion in SPECT-I and -II studies was not significantly higher than the percentage of defects which were worse (57% vs. 33%). The resulting images in SPECT-II, in comparison to preoperative study, presented perfusion improvement less often (33%) than transient defects (78%) but more often than severe persistent defects (18%). They presented no changes in perfusion still less often (40%) than other persistent defects (71%) and more often than transient defects (11%). In summary, those were the defects which early post CABG behaved differently from transient defects as well as from more severe persistent defects and which often became worse three months later.

**Level of perfusion in rest.** Rest uptake of Tc-99m-MIBI in small transient defects theoretically has the closest equivalent in small persistent defects (and only in cases of minor reversibility of small transient defects). Rest uptake of Tc-99m-MIBI in medium transient defects theoretically has the equivalent in medium persistent defects (in cases of minor reversibility) or in small persistent defects (in cases of significant reversibility). Rest uptake of Tc-99m-MIBI in severe transient defects theoretically has the equivalent in severe persistent defects (in cases of minimal reversibility), in medium persistent defects (in cases of significant reversibility) or in small persistent defects (if there was very big reversibility — which was not observed in our study). But, despite similar rest uptake of Tc-99m-MIBI, postoperative state of transient defects was different from persistent defects. In small transient defects, perfusion improvement was more frequent than in small persistent defects (89 v. 51% in SPECT-I and 85 v. 33% in SPECT-II). In medium transient defects, perfusion improvement was more frequent than in small and medium persistent defects (77 v. 40% in SPECT-I and 73 v. 34% in SPECT-II). In severe transient defects, perfusion improvement was more frequent than in medium and severe persistent defects (73 v. 21% in SPECT-I and 79 v. 26% in SPECT-II).

**Changes of perfusion state in patients.** Changes in perfusion in SPECT-I and SPECT-II in relation to SPECT-0, affiliated to patients (not to segments, as above), are shown in Figure 3. Perfusion was better early after CABG than preoperatively in 37 of 43 patients (86%, CI_{95} = 72–95%), was unchanged in 3 patients (7%, CI_{95} = 1–19%), and was worse in 3 patients (7%). Perfusion was better late after CABG than preoperatively in 27 of 36 patients (75%, CI_{95} = 58–88%), was unchanged in 6 patients (17%, CI_{95} = 6–33%), and was worse in 3 patients (8%, CI_{95} = 2–22%). Among 36 patients with both postoperative studies, «concordance» was achieved in 34 patients (94%); in one patient perfusion was better in SPECT-I and worse in SPECT-II (in comparison to SPECT-0) and in another one perfusion was worse in SPECT-I and better in SPECT-II.

**Changes in exercise capacity of the patients.** Patients achieved 6.9 ± 2.7 MET (MET — metabolic equivalent; 1 MET = 3.5 ml O_2 per kg and minute) during stress SPECT-0, 8.3 ± 2.5 MET during SPECT-I (p < 0.01), and 9.7 ± 2.9 MET during SPECT-II (p < 0.01 in comparison to SPECT-I and p < 0.00001 in comparison to SPECT-0). In SPECT-I, exercise capacity increased in 27 of 43 patients (63%, CI_{95} = 48–76%, NS in comparison to the percentage of patients with perfusion improvement) and «concordance» between perfusion and exercise capacity (improvement, preservation or deterioration) was achieved in 26 of 43 patients (60%, CI_{95} = 45–74%) in the early control term. In SPECT-II, exercise capacity increased in 30 of 36 patients (83%, CI_{95} = 67–92%, NS in comparison to the percentage of patients with perfusion improvement) and «concordance» between perfusion and exercise capacity was achieved in 25 of 36 patients (69%, CI_{95} = 53–83%) in the later control term.

**Discussion**

This study shows that in transient perfusion defects, the postoperative perfusion improvement measured during first 5 months after CABG is more frequent than in small persistent defects and than in medium-and-severe defects. Most often perfusion improvement is observed in small transient defects (taking into account 95-percent confidence interval, improvement can happen in over 90% of the defects). In all the types of transient defects, perfusion improvement is most often observed after CABG. In small persistent defects, perfusion improvement and lack of perfusion changes are observed equally often. In medium and severe persistent defects, lack of perfusion changes after CABG is most often observed.

Rest uptake of Tc-99m-MIBI in small transient defects theoretically has the closest equivalent in small persistent defects, rest uptake in medium transient defects — in medium or small persistent defects, and rest uptake in severe transient defects — in severe or medium persistent defects. But we showed that despite similar rest uptake of Tc-99m-MIBI, postoperative state of transient defects was different from persistent defects. So, preoperative assessment of solely rest uptake, which is the basic method of viability assessment with Tc-99m-MIBI proposed in international literature [5–9, 12], does not seem to be justified: if perfusion defect at rest is associated with the presence of even minimal deterioration of perfusion in stress (inducible ischaemia), then in such a defect a higher probability of perfusion improvement after CABG is observed than in persistent defects. These observations are in agreement with Kitsiou et al. [13], who, in stress-rest viability assessment with Tl-201, proved that even at a similar mass of viable myocardial tissue (as reflected by the final thallium content in redistribution-reinjection images), the presence of inducible is-
chaemia is associated with an increased likelihood of functional recovery. They concluded that, although both reversible and mild-to-moderate irreversible thallium defects after stress retain viable myocardium, the identification of reversible thallium defect on stress in an asynergic region more accurately predicts recovery of function after revascularisation.

In the literature it was shown that perfusion Tc-99m-MIBI SPECT studies (in rest) can accurately identify segments with improved contractile function after revascularisation but have lower predictive specificity than low dose dobutamine echocardiography (Bax et al., on the basis of pooled analysis of 10 studies [12]). In that report [12], however, the efficiency of the technique assessing myocardial perfusion and viability was postoperatively evaluated on the basis of function improvement, mainly by echocardiography. Our goal was to investigate solely the myocardial perfusion and to evaluate to what extent the character of perfusion disturbances allows the state of perfusion after CABG to be predicted. Postoperative control study performed in the same way as preoperative Tc-99m-MIBI SPECT study seemed to us the only precise method of evaluation of the changes in perfusion caused by revascularisation. And, despite the fact that the expected clinical result of revascularisation is the functional improvement of the left ventricle, and not only perfusion improvement, the latter is a necessary condition for functional improvement achievement. It is not proved, however, that it is a sufficient condition. Rohns et al., in isolated rabbit hearts, showed that not all levels of reperfusion are equal for optimal myocardial functional recovery: minimal perfusion improvement may result in persistent stunning of myocardium, without improvement of contractility and oxygen consumption [14]. Also in our study, we did not find a high concordance between perfusion improvement and exercise capacity improvement — which may support the idea about blood flow improvement which sometimes is too low to cause functional improvement of a heart and clinical improvement of a patient. Generally, however, smaller contractility disturbances accompany better regional perfusion (although in myocardial stunning, perfusion improvement may be ahead of functional improvement even for 6–12 months after CABG) [15, 16].

Limitations. No quantitative approach to an assessment of defect severity was applied in this work. Quantitative assessment theoretically could be more exact in cases of making decisions about minimal reversibility against nonreversibility. We believe, however, that visual assessment performed by three observers with many years experience in nuclear cardiology and consensus achieved in every SPECT study guarantee reliable grading of defect severity. The quantitative approach also suffers from known limitations and does not work properly, for instance in situations when the defect does not occupy the whole segment.

Conclusions

1. The result of preoperative stress-rest Tc-99m-MIBI SPECT myocardial perfusion study is an exact predictor of the state of perfusion measured early (< 5 months) after CABG. Postoperative regional perfusion improvement depends above all on the type of defect (improvement in every type of transient defect is significantly more probable than in persistent defects) and on defect severity in stress (improvement in small persistent defects is significantly more probable than in medium and severe persistent defects).

2. Concordance of the results from SPECT performed early (< 2 months) and 3 months later is high (87%) so timing during the first 5 months after operation is not crucial for perfusion evaluation.

3. In small persistent defects, changes in perfusion are different than in other types of defects — so it seems unjustified to consider them together with transient defects (as “viable”) or with persistent defects (as “nonviable”).

4. Preoperative viability assessment on the basis of Tc-99m-MIBI study performed solely in rest is unjustified: at the similar perfusion defect at rest, the presence of even minimal inducible ischaemia is associated with increased probability of perfusion improvement after CABG.

References


