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Original

Nuclear imaging techniques in the assessment of myocardial perfusion and function after CABG: does it correlate with CK-MB elevation?

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Abstract

BACKGROUND: An increase of the creatine kinase MB (CK-MB) isoenzyme after cardiac surgery suggests perioperative myocardial infarction. The interpretation is more difficult when increased enzymes are not accompanied by electrocardiographic markers of infarction. The aim of this study was to correlate the results of myocardial perfusion imaging (MPI) and radionuclide ventriculography (RNV) with CK-MB isoenzyme level in patients without ECG abnormalities after CABG.

MATERIAL AND METHODS: 36 patients (age: 52.5 ± 8.5 years, 33M/3F) treated with CABG were prospectively studied. CK-MB level was assessed at 0, 4, 8, 12, 24, 36, 48 and 72 hours after surgery. MPI (SPECT using Tc-99m-MIBI) and RNV were performed 2 weeks before and 3–4 months after surgery. All patients had an uneventful hospitalisation. The subjects were divided into two groups: group 1 with CK-MB increase > 50 IU/ml (n = 9) and group 2 with CK-MB levels ≤ 50 IU/ml (n = 27). There was no difference between the groups regarding the number of diseased arteries, haemodynamic parameters, aortic clamping time or the number of grafts.

RESULTS: Perfusion improvement at stress and at rest was significantly lower in group 1 than in group 2. The ejection fraction did not change significantly in both groups (ΔEF = 0.6 ± 13.5 in group 1 v. 0.7 ± 9.7 in group 2, p = NS), however, in 5 patients from group 1 (56%) and in 6 patients from group 2 (22%) the EF decreased significantly at follow-up RNV (p = 0.05). In 6 patients (5 in group 1 and 1 in group 2) a new defect of perfusion was found at follow-up MPI. The sensitivity and specificity of increased CK-MB level in predicting perfusion deterioration were 83% and 87%, respectively.

CONCLUSIONS: We conclude that patients with an increased level of CK-MB isoenzyme (> 50 IU/ml) after coronary artery surgery have a higher rate of perfusion and function deterioration. The increase of CK-MB level early after coronary bypass surgery in patients without ECG markers of perioperative infarction indicates a probable ischaemic insult during surgery.

Key words: coronary artery bypass grafting, CK-MB isoenzyme, perioperative infarction, myocardial perfusion imaging, radionuclide ventriculography

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Introduction

With the increase of indications for coronary artery bypass grafting (CABG) observed in recent years, an appropriate patient selection and interpretation of diagnostic tests used for quick and correct assessment of ischaemia has become especially important. According to CASS study, perioperative myocardial infarction occurs in 6% of operated patients [1]. Monitoring creatine kinase (CK) activity and — particularly — its isoenzyme CK-MB [2, 3] is routinely employed, since the release of this enzyme into the blood results from the myocardial cell damage. A CK-MB increase above the normal level suggests perioperative infarction especially when it is accompanied by ECG changes [4–6]. However, difficulties in

interpretation appear when the enzyme level increase is not accompanied by specific ischaemic ECG changes [5, 6].

Myocardial perfusion imaging (MPI) and radionuclide ventriculography (RNV) may provide some additional information on the myocardial damage following cardiac surgery [7]. MPI could be useful in diagnosing new perfusion defects. RNV, on the other hand, allows an assessment of left ventricular muscle contractility changes.

The aim of this study was to correlate the results of MPI and RNV with CK-MB isoenzyme level in patients without ECG abnormalities after CABG.

Material and methods

36 patients without electrocardiographic signs of perioperative infarction scheduled for CABG were randomly selected. The group consisted of 33 men and 3 women, aged 34–69 years (mean age 52.5 ± 8.6 years). Before surgery, 27 patients (75%) had at least one myocardial infarction. The other 9 patients complained of typical angina, but no myocardial infarction was diagnosed. Preoperative coronary angiography revealed significant changes in 1 coronary vessel in 3 patients, in 2 vessels in 14 patients, and in 3 vessels in 19 patients.

Creatine kinase (CK) concentration was determined by means of the kinetic method using commercially available reagents by bioMerieux. The myocardial fraction (CK-MB) was measured following immunoinhibition of the M fraction, using a reagent by the same manufacturer. The measurements were performed using a Mascott Plus unit made by LISABIO. In all patients, CK and CK-MB measurements were carried out at 0, 4, 8, 12, 24, 36, 48 and 72 hours after surgery. A CK-MB increase above 50 IU/ml was adopted as a level corresponding to postoperative ischemia.

A 12-lead ECG examination was made before surgery and 6, 12, 24, 48 and 72 hours after the operation.

One week before and 4 to 6 months after surgery MPI and RNV were performed. MPI was carried out according to the two-day protocol, using 99mTc-MIBI. Rest studies were performed using 740 MBq (20 mCi) of 99m-Tc-MIBI (technetium generator by Nycomed-Amersham, MIBI by Polatom, Poland). On the other day, pharmacological stress was performed using dipyridamole (0.56 mg/kg, infused over 4 minutes), followed by the injection of 740 MBq (20 mCi) of 99m-Tc-MIBI. Acquisition of SPECT images started 60–90 min. after the tracer injection. Images were obtained by the single-head Diacam rotation gammacamera (Siemens). Semiquantitative evaluation of the images was based on the assessment of 99m-Tc-MIBI uptake in 9 myocardial segments (2 segments in anterior, lateral, infero-posterior and septal wall and 1 apical segment). The scoring was performed using a 5-point scale, whereas 1 meant normal uptake, 2 — slightly impaired uptake, 3 — moderate defect, 4 — severe defect, 5 — no uptake. Scores obtained in each segment were summed up, constituting the summed defect score at rest (SDS-R) and following stress testing (SDS-S). Improvement or deterioration of the myocardial perfusion after CABG was evaluated by analysing the difference of these parameters after surgery and at baseline (ΔSDS-R, ΔSDS-S).

RNV was performed after in-vivo erythrocyte labelling using 30 mg of stannous pyrophosphate (by Polatom, Poland) followed by the injection of 740 MBq (20 mCi) of 99mTc-pertechnate (Nycomed-Amersham). Gated image acquisition started 10 min. after the last injection using the same gammacamera as in the case of MPI studies. Typical LAO 30–45° projection with 5–10° caudal tilt and 24-sequence gating were used during the acquisition. Left ventricular ejection fraction (EF) was then calculated using semi-automatic method.

All operations were carried out as scheduled by the same team of surgeons and anaesthesiologists, in extracorporeal circulation, at moderate hypothermia (28–30°C), using crystaloid St Thomas cardioplegia, administered to the aortic root. Stenosed left anterior descending (LAD) or diagonal I (Dg I) artery was revascularised using the left internal thoracic artery (LITA). Right coronary (RCA), left circumflex (Cx), marginal (Mg), Dg and LAD artery were revascularised utilising the saphenous vein.

Depending on the maximal postoperative CK-MB level, the patients were classified into one of two groups:

Group 1 with CK-MB maximum $>$ 50 IU/ml; n = 9 patients

Group 2 with CK-MB maximum $\leq$ 50 IU/ml; n = 27 patients.

In statistical calculations, continuous variables were expressed as a mean value ± standard deviation. The statistical analysis was based on the t-student test for dependent variables and the Wilcoxon rank sum test. The correlations between the analysed parameters were assessed using Spearman's rank correlation coefficient r_s. P values < 0.05 were treated as significant.

Results

No significant difference was found between group 1 (n = 9) and group 2 (n = 27) regarding patient age, preoperative infarction history and cardiac index (Table 1). In 36 patients, 79 significantly stenosed coronary arteries were revascularised — with 1 graft in 5 patients, 2 grafts in 22 patients, 3 grafts in 6 patients and 4 grafts in 3 patients. There was no statistical difference between the groups with regard to the number of stenosed arteries, number of grafts, as well as the end-diastolic pressure (EDP) and end-diastolic volume index (EDVI) measured during cardiac catheterisation. Also the aortal clamping time was similar in both groups (Table 2). In the postoperative period, in none of the patients did ECG reveal any signs of persisted ischaemia.

Due to classification criteria, the maximal CK-MB level in patients from group 1 was above 50 UI/ml (mean value: 70 ± 14). The maximal increase was registered between 8 and 24 hours after surgery (Fig. 1). Over the next hours, the level decreased to 50 IU/ml between 36 and 48 hours after the operation. In group 2, the CK-MB level did not exceed 50 IU/ml (mean value: 24 ± 11), reaching a maximum at zero hour to be followed by a decrease after 24–36 hours and by an insignificant increase after 48––72 hours (Fig. 2).

Table 1. Preoperative data of patients in both groups

	Group 1 (n = 9)	Group 2 (n = 27)	p
Sex	8 M/1 F	25 M/2 F	
Age	53.3 ± 9.9	52.3 ± 8.3	NS
Cardiac index	3.5 ± 1.9	3.7 ± 1.3	NS
History of MI	7 (78%)	23 (85%)	NS

Table 2. Different parameters obtained at cardiac catheterisation, RNV, MPI and operation data in both groups

Parameter	Group 1	Group 2	p
Cardiac catheterisation			
Number of stenosed arteries (n)	2.6 ± 0.5	2.4 ± 0.7	NS
End-diastolic Pressure — EDP [mm Hg]	17.8 ± 11.2	13.0 ± 5.3	NS
End-diastolic Volume Index — EDVI [ml/m^2]	75.4 ± 25.9	79.1 ± 24.5	NS
CABG			
Number of grafts (n)	2.2 ± 0.8	2.1 ± 0.7	NS
Clamping time [min]	62.6 ± 21.0	58.3 ± 19.0	NS
Mean CPK [IU/ml]	3490 ± 2965	981 ± 635	**0.0002**
Mean CK-MB [IU/ml]	70 ± 14	24 ± 11	**0.0001**
RNV			
Ejection Fraction — EF before CABG (%)	55.4 ± 16.0	55.5 ± 13.9	NS
Ejection Fraction — EF after CABG (%)	55.1 ± 17.3	54.8 ± 12.9	NS
ΔEF	0.6 ± 13.5	–0.7 ± 9.7	NS
Number of patients with EF decrease after CABG	5 (56%)	6 (22%)	**0.05**
MPI			
ΔSDS-S (stress)	0.07 ± 0.52	0.84 ± 0.63	0.003
ΔSDS-R (rest)	0.09 ± 0.30	0.38 ± 0.34	**0.04**
Number of segments showing perfusion improvement at stress	0.40 ± 2.70	4.60 ± 3.70	**< 0.006**
Number of segments showing perfusion improvement at rest	0.70 ± 2.40	2.40 ± 2.40	**NS**
Number of patients with new perfusion defects	5 (56%)	1 (4%)	**< 0.002**

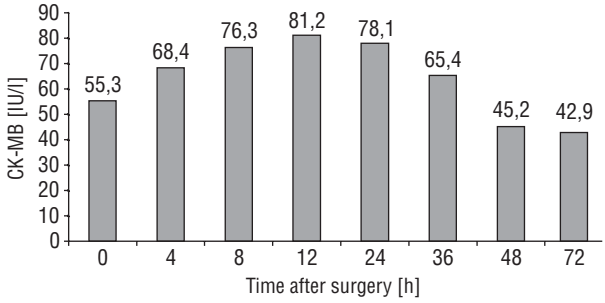

Figure 1. Mean CK-MB level during perioperative period in group 1.

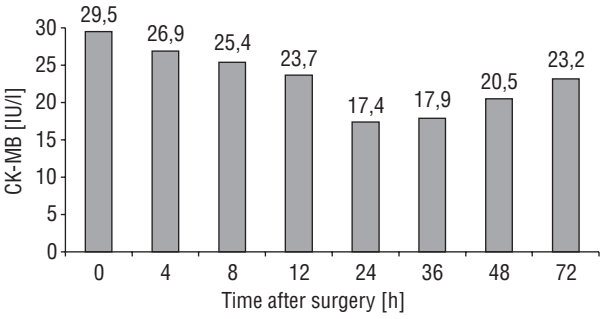

Figure 2. Mean CK-MB level during perioperative period in group 2.

The results of cardiac catheterisation, SPECT and RNV, before and after surgery, are presented in Table 2.

Four months after surgery, group 1 manifested less perfusion improvement than group 2 as assessed with the means of MPI — both at rest and after pharmacological stress — which was expressed by a significantly lower ΔSDS-S and ΔSDS-R in group 1 compared to group 2. Patients from group 1 also had a significantly lower number of myocardial segments showing perfusion improvement at stress images after CABG. A new perfusion defect (i.e. which was absent at the baseline study and occurred at the follow-up MPI) was found in 5 patients (56%) from group 1 and in 1 patient (4%) from group 2.

There was no difference in EF between both groups at baseline and follow-up RNV. Neither did mean EF change significantly following CABG. However, in 5 patients (56%) of group 1 and in 6 patients (22%) of group 2 a decrease of EF by more than 5% was found. These were the same 5 patients belonging to group 1 who had new perfusion defects detected at the MPI.

A significant negative correlation was found between the maximal CK-MB concentration and number of segments with perfusion improvement at stress MPI (correlation factor r = –0.49; p = 0.004) (Fig. 3). However, no statistical correlation was observed between CK-MB maximal concentration and the aortic cross clamping time (r = 0.23; p = 0.2) or the number of grafts (r = 0.19; p = 0.3) (Fig. 4).

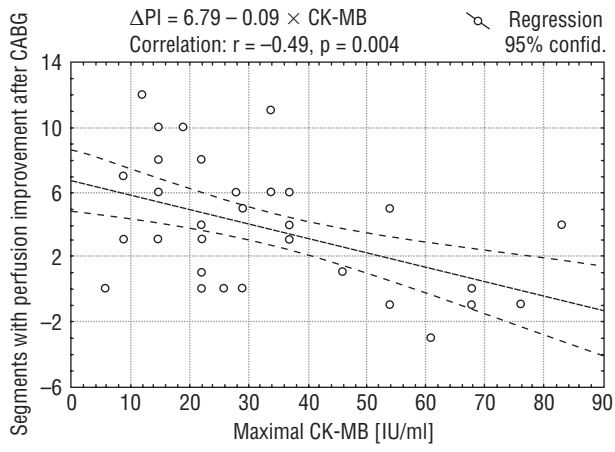

Figure 3. Correlation between CK-MB maximal concentration and number of segments with perfusion improvement after CABG.

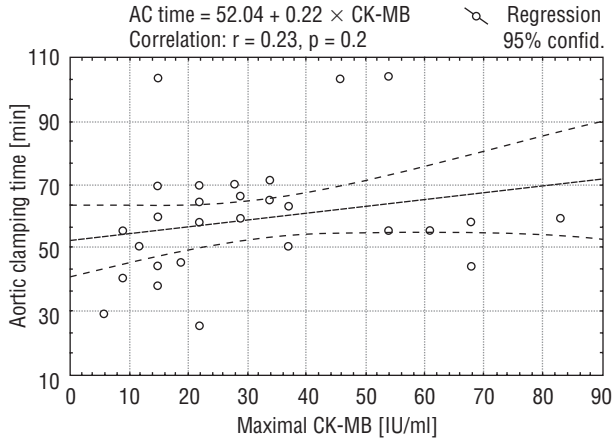

Figure 4. Correlation between the maximal CK-MB concentration and the aortic cross clamping time.

Out of the parameters analysed, only the postoperative CK-MB increase (> 50 IU/ml) was an independent predictive factor of the appearance of new perfusion defects in MPI according to the discrimination analysis (p = 0.01). No such dependence was found for CPK increase.

The value of postoperative CK-MB increase in the detection of persisted myocardial ischaemia, treating myocardial perfusion scintigraphy as a verifying method, was as follows:

— sensitivity: 83%,
— specificity: 87%,
— positive predictive value: 56%,
— negative predictive value: 96%.

Discussion

The aim of myocardial revascularisation is to improve the myocardial perfusion and — thus — alleviate the symptoms of ischaemia as well as to prevent such consequences as myocardial infarction or sudden death [8–11]. Recent years have brought a significant progress in diagnostics of ischaemic heart disease and in coronary by-pass surgery. This has resulted in an increased number of patients qualified to surgery in whom previously surgical treatment would not have been considered due to a high risk of postoperative complications. Most of these patients presented with severely impaired ventricular function, i.e. EF less than 25% [12–15].

Perioperative myocardial damage (infarction) has a significant effect on the early clinical course following surgery and further prognosis. According to CASS study, 6 % of patients operated on are found with perioperative myocardial infarction [1] and it is an important and independent factor in long-term survival rates after CABG. The diagnosis of perioperational myocardial infarction is difficult. The latest findings have shown that the presence of pathological Q waves in ECG is quite specific but not sensitive enough and is not sufficient to establish an accurate diagnosis [4, 7, 16, 17]. An increased concentration of CK-MB alone is a sensitive but not specific criterion. MPI yields a higher incidence of perioperative infarction than ECG alone [7].

In this study, ECG tests and enzymatic (CPK, CK-MB) investigations were conducted in order to monitor perioperative ischaemia. ECG changes (a new Q wave wider than 0.04 s; an ST depression > 2 mm in the precordial leads; a deep T wave inversion persisting more than 48 hours; ventricular tachycardia; ventricular fibrillation) and the simultaneous CK-MB level increase the sensitivity of diagnosing permanent myocardial damage [5]. Diagnosis of perioperative myocardial infarction is not so unequivocal, when the CK-MB level elevation is not accompanied by electrocardiographic signs of infarction. According to Jain [5], 46% of patients after CABG, who manifested electrocardiographic markers of infarction, were also found to have elevated enzyme levels, but only in 17% of patients with enzymatic markers of perioperative myocardial damage did characteristic changes in ECG occur. The CK-MB increase after CABG might have resulted from many factors, independent of perioperative ischaemic myocardial damage. According to Hippellainen [18] and Greaves [7], such independent factors are: the number of defibrillations for restoration of the sinal rhythm, aortic clamping time > 100 minutes, cardiac fibrillation time before and after aortic clamping, total time of extracorporeal circulation, number of anastomoses and incomplete revascularisation, myocardial infarction in the preceding week and previous revascularisation. Our study, however, did not confirm the effect of aortic clamping time and the number of grafts on the CK-MB level.

The CK-MB level increases most considerably 16 hours after surgery, on average [5], which was also confirmed in this investigation (between 12 to 24 hrs. after CABG).

According to Huseby [19] and Farah [20], a CK-MB (> 50 IU/ml) increase 20 hours after CABG is indicative of perioperative myocardial infarction. In 1998, the American College of Cardiology, using data from numerous US and Canadian centres [4], reported that a threefold or greater increase in CK-MB level after PTCA and a fivefold or greater increase after CABG above the standard value are connected with significant perioperative myocardial damage.

In the present study, MPI and RNV performed four months after surgery in patients with postoperative CK-MB elevation > 50 IU/ml revealed no significant perfusion improvement. Moreover there were new perfusion defects not observed prior to surgery as well as contractility disorders. The results have confirmed that – even though there were no characteristic ischaemic changes in the ECG examination – an increase in CK-MB level during the perioperative period is indicative of significant and permanent myocardial damage.

Conclusions

An elevation of myocardial fraction of creatine kinase (CK-MB) > 50 IU/ml during the postoperative period after CABG in patients without electrocardiographic signs of myocardial infarction, is connected with:

— a lower rate of perfusion improvement;
— a more frequent occurrence of a new defect at MPI;
— a more frequent decrease of ejection fraction.

Thus, the increase of CK-MB early after CABG in patients without ECG signs of perioperational infarction indicates a probable ischaemic insult during surgery.

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