Magnetic Resonance *versus* Technetium-99m Pyrophosphate Scintigraphy in the Detection of Perioperative Myocardial Necrosis

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Summary

Background: Perioperative myocardial infarction (POMI) is a complication of coronary artery bypass grafting (CABG) with a potential prognostic impact. Technetium-99m pyrophosphate myocardial scintigraphy (MS) is used in the diagnosis of POMI; however it shows a limited sensitivity for subendocardial lesions. Cardiovascular magnetic resonance imaging (CMRI), in turn, has a high accuracy in the detection of myocardial necrosis.

Objective: To compare CMRI and MS for the detection of POMI after CABG.

Methods: A total of 24 patients with chronic coronary artery disease were studied using the delayed contrast enhanced CMRI and MS before and after CABG by analyzing the development of areas of perioperative myocardial necrosis (POMI). Biochemical markers of myocardial injury (CKMB and troponin I) were also determined before and after surgery.

Results: Nineteen patients completed the study. Of these, 6 (32%) presented POMI on CMRI and 4 (21%) on MS (p = NS). Of the 323 left ventricular segments assessed, 17 (5.3%) showed perioperative necrosis on CMRI and 7 (2.2%) on MS (p = 0.013). Moderate agreement was observed between the methods (kappa = 0.46). There was disagreement regarding the diagnosis of POMI in 4 (21%) cases, most of them with small areas of perioperative necrosis on CMRI which were not visualized on MS. In all cases with POMI on CMRI, significant CKMB and troponin I elevations were observed.

Conclusion: Moderate diagnostic agreement was observed between the methods for the detection of POMI, but CMRI enabled visualization of small areas of perioperative myocardial necrosis which were not identified on MS and were associated with elevation of biochemical markers of myocardial injury. (Arq Bras Cardiol 2008;91(2):113-118)

Key words: Comparative studies; magnetic resonance imaging; myocardial/radionuclide imaging; technetium Tc99m pyrophosphate; myocardial infarction/surgery; myocardial revascularization.

Introduction

Despite the advances in surgical techniques and intensive care, perioperative myocardial infarction (POMI) is still a complication of coronary artery bypass grafting (CABG), with a potential prognostic impact[1-5]. Among the tests used for its diagnosis, technetium-99m pyrophosphate myocardial scintigraphy (MS) stands out as a noninvasive method able to visualize areas of myocardial necrosis[6]. Despite its good sensitivity in detecting transmural infarction, planar scintigraphy has a low sensitivity in detecting subendocardial infarction, which is the most common type following CABG[7]. The single-photon emission computed tomography technique, better known as SPECT, has a higher sensitivity in detecting subendocardial infarction; however its specificity is also limited[6]. Additionally, the test remains positive for a relatively short time, approximately seven days[7-9], based on the radionuclide binding to mitochondrial calcium of myocytes affected by the infarction, and this may limit its use within the first postoperative days in clinically unstable patients who cannot be transferred to the Nuclear Medicine department.

Cardiovascular magnetic resonance imaging (CMRI), in turn, has become the gold-standard test for visualization of areas of infarction with the delayed myocardial contrast enhancement technique. This method uses a specific sequence performed 10 to 20 minutes after the intravenous administration of gadolinium-based contrast medium; gadolinium is a paramagnetic metal able to enhance the signal intensity of structures in resonance imaging[10]. Through this method, accurate determination of recent or old infarction areas has been possible both in animals and humans, with or without Q-wave on ECG[11], and even of microinfarctions without electrocardiographic or wall motion changes and mild cardiac enzyme elevation[12]. This technique has a high spatial resolution, higher than that of scintigraphy, and a strong correlation with pathological anatomy in experimental studies in animals[13,14].

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Based on these facts, and in light of the lack, to date, of comparative studies between these methods, we conceived this study, whose objective was to evaluate the diagnostic agreement between CMRI and MS for the detection of POMI areas in patients undergoing CABG.

Methods

Between August 2003 and March 2006, 24 adult patients with chronic coronary artery disease followed up in our institution and with indication for coronary artery bypass grafting were studied. All cases underwent conventional coronary angiography, and critical stenosis was observed in at least one coronary artery (≥ 50% for the left main coronary artery and ≥ 70% for any of the other arteries). Exclusion criteria were the following: planning of another cardiac surgical treatment in addition to coronary artery bypass grafting (heart valve replacement, for instance); chronic heart arrhythmias that could affect CMRI image acquisition (atrial fibrillation, for instance); and contraindications for magnetic resonance imaging (pacemaker / implantable cardioverter-defibrillator, metallic implants or prostheses not compatible with the imaging test, allergy to gadolinium, and known claustrophobia). The study was approved by the Institution's Ethics Committee and a written informed consent was obtained from all patients.

The patients underwent CMRI and MS before and after surgery to evaluate the development of perioperative areas of myocardial necrosis. Biochemical markers of myocardial injury (CKMB and troponin I) were also measured before, and serially after surgery.

Cardiovascular magnetic resonance imaging

The tests were performed in a 1.5 T magnetic MRI scanner (Signa CV/i, General Electric Medical Systems, Waukesha, MN, USA), using a commercially available four-element cardiac-phased array surface coil. For electrocardiographic monitoring and gating, four electrodes were attached to the patient's left anterior chest wall. All tests were obtained with expiratory breath-hold so as to minimize the artifacts resulting from respiratory movements. Initially, acquisitions were made in the three orthogonal planes (axial, sagittal and coronal) to locate the heart. From these preliminary images, the prescription of the delayed myocardial enhancement sequence was planned. Left ventricular (LV) short-axis and long-axis view planes were generated. The short-axis views were acquired with 8-mm width and spaced at 2-mm intervals, in a sufficient number (8 to 12) to cover all the extent of the LV. The long-axis views were planned from the short-axis images, with 8-mm width and spaced at 45º radial intervals, in a total of four views. In order to ensure comparability, the images were acquired in the same view planes before and after surgery. For the assessment of areas of myocardial necrosis and fibrosis, a specific fast gradient-echo sequence with inversion-recovery preparatory pulse was used. The images were acquired approximately 10 to 20 minutes after intravenous administration of 0.2 mmol/kg of gadolinium contrast (gadoteric acid, Dotarem™, *Guerbet, Aulnay Sous Bois*, France), via peripheral venous access, at every two heart beats (RR intervals) and the inversion time was carefully adjusted with the purpose of nulling the normal myocardial signal. The main parameters of this sequence were: TR=7.2 ms, TE=3.2 ms, matrix=256x192 pixels, flip angle=20°, bandwidth=31.2 kHz, TI=150-250 ms, field of view=34-38 cm.

The images were analyzed using the CineTool version 3.4 program (General Electric Medical Systems) by one observer (G.U.M.) who was blinded to the clinical characteristics of the patients, as well as to the findings of the other diagnostic methods. Only the areas of delayed myocardial contrast enhancement (necrosis / fibrosis) with signal intensity greater than two standard deviations above the mean value of myocardial signal intensity in a remote area considered normal according to a methodology described elsewhere[15] were delimited. The 1.05 g/cm^3 value of myocardial density was used for the calculation of the infarcted mass. POMI was defined as the finding of a new area of delayed myocardial contrast enhancement in the postoperative test that was not present in the imaging test performed before surgery. The segmental analysis followed the pattern of myocardial segmentation recommended by the American Heart Association, which defines the division of the LV in 17 segments: six basal, six mid-cavity, four apical segments, and the apex[16].

Myocardial scintigraphy

The tests were acquired in tomographic mode (SPECT), on an ADAC Forte dual-headed gamma camera (Philips Medical Systems, Milpitas, CA, USA), approximately three hours after intravenous administration of 740 MBq (20 mCi) of the radionuclide (pyrophosphate-^{99m}Tc, supplied by *Instituto de Pesquisas Energéticas e Nucleares* – IPEN, Sao Paulo, SP, Brazil). During the test, the patients remained in the supine position. A high-resolution collimator was used, 360° orbit, with 96 views and 30 seconds per view, 64x64 pixel matrix, with counting acquisition at the 140 keV photopeak of tecnecium-99m and 15% energy window. The images were reconstructed in the orthogonal planes (axial, coronal and sagittal) using iterative reconstruction with five iterations. Considering the period during which pyrophosphate uptake is positive, the postoperative test was performed up to the seventh day after surgery. In patients who presented clinical decompensation that impeded their transfer to the Nuclear Medicine department within this time interval, the postoperative test was not performed. The decision regarding the possibility of transfer was left to the discretion of the physicians in charge of the postoperative care of the patients.

Image interpretation was made by a consensus between two observers (M.I. and J.C.M.) who were blind to the clinical characteristics of the patients, as well as to the findings of the other diagnostic methods. The pre and postoperative tests were compared, and the development of focal areas of anomalous radionuclide accumulation after surgery was recorded, following the same 17-segment model used for the analysis of CMR images.

Biochemical markers of myocardial injury

CKMB and troponin I levels were determined using specific kits in the Immulite™ 1000 analytical system (Diagnostic Products Corporation, Los Angeles, CA, USA). Reference values for these tests are of up to 4.0 ng/mL for CKMB and up to 1.0 μg/L for troponin I. Blood samples for CKMB determination were collected prior to surgery; every six hours after surgery, until the peak elevation was determined; and every 24 hours from then on, until discharge from the ICU. The samples for troponin I determination were collected before surgery; every eight hours after surgery, until the peak elevation was determined; and every 24 hours from then on, until discharge from the ICU. In two cases, blood samples for serial troponin could not be collected after surgery due to operational reasons. Upper limit of normal[17] elevations of biomarkers greater than fivefold were considered significant both for CKMB and troponin I.

Statistical analysis

The statistical analysis was made using the SPSS for Windows version 10.0 program. Continuous variables were expressed as mean ± standard deviation and categorical variables were described as frequencies. The McNemar's test was used for comparison of the frequency of the diagnosis of POMI between CMRI and MS, and the kappa statistics was used to verify the agreement between the methods.

Results

Nineteen patients completed the study. Of these, the majority (84%) were males. The mean age was 63 ± 10 years. In five (21%) out of the 24 patients included, postoperative MS could not be performed within the seven days following surgery (estimated period of pyrophosphate uptake): four due to clinical complications that impaired their transfer to the Nuclear Medicine department and one case due to technical problems.

Cardiovascular magnetic resonance imaging

The preoperative test was performed on average 16 ± 15 days before surgery and the postoperative test, 10 ± 8 days after surgery. Of the 19 patients, six (32%) presented new areas of delayed LV myocardial contrast enhancement in the postoperative test that were not previously present, and were compatible with perioperative lesions. Most of these areas were small and had a focal distribution. Despite this fact, a significant elevation of the biochemical markers of at least tenfold the upper limit of normal was observed in all cases with perioperative necrosis on CMRI (Table 1). According to the segmental analysis, development of perioperative myocardial necrosis was observed in 17 (5.3%) of the 323 LV segments assessed.

Myocardial scintigraphy

The preoperative test was performed on average 18 ± 15 days before surgery and the postoperative test, 5 ± 2 days after surgery. Of the 19 patients, four (21%) presented an anomalous LV area of pyrophosphate accumulation in the postoperative test, thus indicating perioperative myocardial necrosis. In the segmental analysis, development of perioperative necrosis was observed in seven (2.2%) of the 323 LV segments assessed.

Biochemical markers of myocardial necrosis

Eleven (58%) of the 19 patients who completed the study presented significant postoperative CKMB elevation and nine (53%) of 17 patients presented significant troponin I elevation (Table 1). As previously mentioned, all cases with perioperative necrosis on CMRI presented significant postoperative elevation of serum levels of the biochemical markers of at least tenfold the upper limit of normal. On the other hand, in one of the patients who presented postoperative radionuclide uptake on scintigraphy, neither significant CKMB elevation was observed, nor was delayed contrast enhancement detected on CMRI. As can be observed on Table 1, in five (38%) of the 13 patients with no perioperative areas of necrosis on CMRI, and in eight (53%) of the 15 patients with no anomalous radionuclide uptake, significant CKMB elevations were observed after surgery. Likewise, in four (33%) of 12 patients with negative CMRI for perioperative myocardial infarction (MI) and in six (43%) of 14 patients with negative scintigraphy for perioperative MI, significant postoperative troponin I elevations were observed.

Comparison between methods

Overall, there was moderate diagnostic agreement between the methods – kappa = 0.46 (Figure 1). There was disagreement between CMRI and MS regarding the diagnosis of POMI in four (21%) cases. In three of them,

Figure 1 - Correspondence between the finding of perioperative myocardial necrosis on CMRI and on technetium-99m pyrophosphate myocardial scintigraphy in one of the patients studied. A: preoperative short-axis resonance image, without areas of delayed myocardial contrast enhancement. B: postoperative short-axis resonance image showing focal injury in left ventricular medial inferoseptal segment (arrow). C: postoperative scintigraphy showing radionuclide uptake in the same segment (arrow).

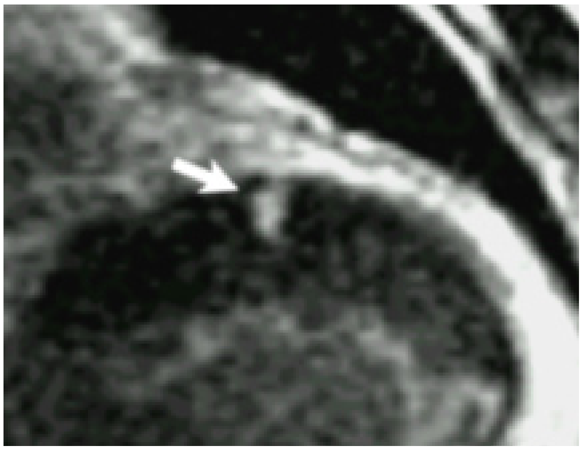

Figure 2 - Small focal area of perioperative myocardial necrosis (arrow) in the left ventricular medial anterior segment detected on CMRI and not visualized on technetium-99m pyrophosphate myocardial scintigraphy in one of the patients studied.

perioperative necrosis was observed on CMRI; however, anomalous pyrophosphate accumulation was not observed on MS (Figure 2). In these cases, the infarcted mass, as measured by CMRI, was small (mean of 1.8 g). In the other case, postoperative radionuclide uptake was observed despite the absence of new areas of delayed myocardial contrast enhancement on CMRI. This patient did not progress with significant CKMB elevation after surgery (Table 1).

Although CMRI had detected POMI in a greater proportion of patients than did MS, this difference was not statistically significant ($p = 0.625$). However, considering the LV segmental analysis, CMRI detected perioperative myocardial necrosis in a significantly greater proportion of segments than did MS (17 [5.3%] versus 7 [2.2%]; $p = 0.013$). In most of the cases, these segments presented small areas of delayed myocardial contrast enhancement with a predominantly focal distribution.

Discussion

This is one of the first studies to use delayed contrast enhanced CMRI for the detection of POMI, and to compare

Table 1 – Findings of magnetic resonance imaging, myocardial scintigraphy and biochemical markers of myocardial injury in the patients studied

Case	Magnetic resonance imaging			Myocardial scintigraphy		Significant elevation* of biochemical markers (peak)	
	POMI	N segments affected	POMI mass (g)	POMI	N segments affected	CKMB	Troponin I
1	Y	1	2.1	Y	1	Y**	Y**
2	N	0	0	N	0	N	N
3	Y	2	3.6	Y	1	Y**	Y**
4	N	0	0	N	0	N	N
5	Y	8	30.7	Y	4	Y**	Y**
6	N	0	0	N	0	Y	Y**
7	Y	1	1.1	N	0	Y**	Y**
8	N	0	0	N	0	N	N
9	N	0	0	N	0	Y	N
10	N	0	0	N	0	N	N
11	N	0	0	N	0	Y**	Y**
12	Y	1	0.7	N	0	Y**	Y**
13	N	0	0	N	0	Y**	Y**
14	N	0	0	N	0	N	N
15	N	0	0	N	0	N	Y
16	N	0	0	N	0	N	N
17	N	0	0	Y	1	N	...
18	N	0	0	N	0	Y	N
19	Y	4	3.6	N	0	Y**	...

**>5x the upper normal limit; **≥10x the upper normal limit; Y: yes N: no.*

this technique with technetium-99m pyrophosphate myocardial scintigraphy for the detection of necrosis. A moderate diagnostic agreement was demonstrated between the two methods, but CMRI allowed the visualization of areas of perioperative myocardial necrosis in a greater proportion of patients and of left ventricular segments.

Disagreement between the tests was mainly observed in the cases with small perioperative infarctions on CMRI not identified on MS. Taking the greater spatial resolution of CMRI into consideration, these were more likely false-negative results of scintigraphy. This hypothesis is supported by the significant elevation (at least tenfold the normal limit) of serum biomarkers observed in these cases. In an experimental study, Wagner et al[14] compared delayed contrast-enhanced CMRI with dual (thalium-201 and sestamibi-^{99m}Tc) scintigraphy (SPECT) for the detection of myocardial infarction in dogs, using pathological anatomy as a reference. The methods were similar for the identification of transmural infarction; however, scintigraphy was less accurate than CMRI in detecting smaller subendocardial infarcts[14]. This is probably also valid in relation to the results found in the present study. Postoperative pyrophosphate uptake was observed in one case without the development of a new area of delayed myocardial contrast enhancement on CMRI. Although a false-negative CMRI result could not be ruled out, the progression of the biochemical markers (absence of significant CKMB elevation) once again suggests diagnostic failure of scintigraphy. Pyrophosphate persistence in the blood pool is one of the possible causes of false-positive results of this test[18].

Although the difference, in favor of CMRI, had occurred in function of small POMI areas, our group has recently demonstrated that small perioperative areas of myocardial necrosis as detected by CMRI have a short and mid-term impact on the LV systolic function[19]. However, there is no evidence, to date, that these small POMI areas determine a poorer clinical outcome. On the other hand, in all cases with perioperative injury on CMRI, a significant elevation of serum levels of biochemical markers of myocardial injury (CKMB and troponin I) of at least tenfold the normal limit was observed. Large studies recently published proved the association of significant increases in CKMB after surgery with a poorer long-term prognosis, with higher incidence of cardiovascular events and lower survival[5,20].

Limitations

Despite these encouraging results, some limitations of the present study have to be recognized. The first and major limitation is the small case series, which may have masked differences between the methods and limited the magnitude of the disagreements observed. This is the case of the difference regarding the frequency of detection of POMI per patient, since the power of the study was not wide enough to reach statistical significance. Second, in some cases, scintigraphy could only be performed on the seventh postoperative day due to clinical restrictions of the patients, which may have reduced the test sensitivity. The relatively short period during which pyrophosphate uptake is positive following the occurrence of myocardial necrosis may limit its utilization for the diagnosis of POMI, since clinical instability is not uncommon on the first postoperative days, thus impeding the performance of the test. In fact, in this study, four patients could not be transferred to the place where the test was performed within the predetermined period of seven days and, therefore, they did not undergo postoperative scintigraphy. An option would be the use of planar scintigraphy, which can be performed at bedside. However, its sensitivity is known to be lower than that of tomographic acquisition (SPECT) for the detection of non-transmural infarcts[7], which are the most common in the perioperative setting. Also, the prolonged pyrophosphate persistence in the blood pool verified in some cases may have influenced the accuracy of the tests, thus partially limiting the diagnostic quality of the images.

Finally, it is necessary to underscore some current limitations of CMRI, which can reduce its clinical applicability in the perioperative setting: prolonged time for image acquisition, high costs and low availability, in addition to the contraindications to its performance, which were listed in the exclusion criteria of this study. Under these conditions, myocardial scintigraphy for the detection of necrosis, along with the other clinical parameters, remains an option for the diagnosis of POMI.

Conclusion

Moderate diagnostic agreement was observed between CMRI and MS in detecting perioperative myocardial necrosis. Greater disagreement was observed in patients with small POMI areas on CMRI that were not identified on scintigraphy and were associated with the elevation of biochemical markers of myocardial injury, thus suggesting that these were false-negative MS results. CMRI still shows some limitations regarding its routine use in the perioperative setting. However, the improvement of the delayed myocardial contrast-enhanced technique, especially with three-dimensional sequences of fast acquisition[21] may broaden the potential of application of this method in the assessment of patients undergoing cardiac surgery.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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Study Association

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