Detection of Perioperative Myocardial Damage after Coronary Artery Bypass Graft Surgery

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SUMMARY In order to evaluate methods for detecting perioperative myocardial damage we studied 41 patients before and serially following coronary artery bypass graft surgery utilizing the 12-lead ECG, serum MB-CPK measurements, and 99mTc pyrophosphate myocardial scans. Six of the 41 patients (15%) developed persistent new Q waves after surgery. Six other patients demonstrated ischemic ST-T wave changes that persisted for 48 hours or more. Mean total MB-CPK released was highest for the group with new Q waves [1598 ± 545 (se) I.U./L • hr] as compared to the group with ischemic ST-T wave changes [708 ± 65 I.U./L • hr] or the group with no ECG changes [262 ± 47 I.U./L • hr]. Ten patients (24%) had positive postoperative pyrophosphate scans consistent with myocardial infarction. The three techniques were compared in these 41 patients utilizing 465 I.U./L • hr as the upper limit of normal MB-CPK released after uncomplicated coronary bypass surgery (no ECG changes, negative scan). Five patients with ischemic ECG changes had a positive scan and high MB-CPK; six patients with no ECG changes had high MB-CPK but a negative scan; and one patient with high MB-CPK and new Q wave had a negative scan. We conclude 1) new Q waves on ECG underestimate the incidence of myocardial damage after coronary artery surgery; 2) MB-CPK alone overestimates the incidence of infarction; and 3) a combination of the three techniques is the best means for detecting myocardial damage after coronary artery bypass graft surgery.

MYOCARDIAL INFARCTION following coronary artery bypass graft surgery is usually associated with increased mortality and morbidity, but definite figures on its incidence have been difficult to obtain because of problems in making a reliable diagnosis. The incidence of electrocardiographic (ECG) and vectorcardiographic findings consistent with postoperative myocardial infarction has ranged from 6 to over 40% in various series. However, problems with the interpretation of the postoperative ECG limit its usefulness. Various serum enzymes have been used in an attempt to detect myocardial damage after coronary artery surgery. Unfortunately, the serum concentrations of CPK, GOT and LDH are all elevated postoperatively due to skeletal muscle trauma, and the degree of elevation of these serum enzymes is not a reliable indicator of myocardial infarction.

The heart specific or MB-isoenzyme of CPK may be more useful for the detection of infarction after coronary bypass surgery. In addition, myocardial infarction imaging with such agents as technetium-99m labeled pyrophosphate has been advocated for the detection of acute myocardial infarction. For these reasons, we designed a protocol to evaluate the relative usefulness of the electrocardiogram, MB-CPK serum levels, and pyrophosphate scanning for the detection of myocardial damage early after coronary artery bypass graft surgery.

Methods

The study population consisted of 41 patients who underwent elective saphenous vein bypass grafting as an isolated procedure for symptomatic coronary artery disease. There were 34 males and seven females with a mean age of 56 years (range 37 to 74). The operative technique utilized was essentially the same for every patient with the exception that 11 patients had a right coronary artery mechanical endarterectomy in addition to bypass grafting of this vessel. Moderate hypothermia (30 to 33°C) and electrical fibrillation and defibrillation of the heart were used. In each case aortic cross-clamping was performed for short periods during the procedure and direct perfusion of the coronary arteries was not performed. Venting was accomplished through a pulmonary vein unless there was a definite left ventricular scar through which the drain could be placed.

A standard 12-lead electrocardiogram was obtained in each patient the day prior to surgery, immediately following...
operation, at 12, 24, 48 and 72 hours after operation and on the day prior to hospital discharge. All ECGs were analyzed independently by two observers, one of whom was not familiar with the patients, and a third observer resolved any differences of opinion. New persistent Q waves in three contiguous leads, one of which was at least 0.04 seconds in duration, in the absence of a conduction abnormality or marked shift in QRS axis, were considered indicative of myocardial infarction. Horizontal ST-segment depression of one millimeter or more, associated with T wave inversion in two or more adjacent ECG leads, that persisted for at least 48 hours was considered a significant change suggestive of ischemia. No patient with ischemic ECG changes received digitalis. Other ST-T wave changes were considered non-specific.

Blood for analysis of cardiac enzymes was obtained the day prior to surgery and serially at 8, 12, 24, 48 and 72 hours after surgery. Total serum CK activity was measured by a modification of the method of Rosalki employing a Cal-Biochem Stat-Pak with incubation at 30° C. MB-CPK was identified by a fluorescent technique after being separated by electrophoresis on cellulose acetate strips, and MB-CPK was then expressed in international units per liter (I.U./L) after relating the percent MB-CPK to the total serum CPK.

In order to obtain an approximation of the total amount of MB-CPK released postoperatively the area described by a line connecting each MB-CPK value (Y) at each sampling time(t) was calculated using the following equation for the sum of successive trapezoids:

\[ \text{MB-CPK area} = \frac{6}{2} \sum_{i=1}^{n} (Y_{i+1} + Y_i) (t_{i+1} - t_i) \]

where \( Y_i \) = MB-CPK value at time \( t_i \). The resultant MB-CPK area was expressed as I.U./L \cdot hours. A more accurate estimation of total amount of MB-CPK released was not possible because the long interval between samples precluded estimation of the fractional disappearance rate of MB-CPK from the circulation.

Pyrophosphate scans were obtained in all 41 patients 3 to 6 (average 5 days) following surgery and 26 of these patients

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<th>Table 1. Pre and Postoperative Data on All 41 Patients</th>
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Abbreviations: N = normal; "N" = nonspecific ST-T wave changes; MI = myocardial infarction; I = inferior; P = posterior; A = anterior; AL = anterolateral; AS = anteroseptal; RBBB = right bundle branch block; LAD = left axis deviation; LVH = left ventricular hypertrophy; 1°AVB = first degree atrioventricular block.
had preoperative scans done as well. Imaging was performed with a gamma scintillation camera in the anterior, lateral, and 45° left anterior oblique projections two to three hours after the intravenous administration 15 mCi of \(^{99m}\text{Tc}\) pyrophosphate. All scintigrams were recorded on polaroid film and were examined independently by two observers, one of whom was unfamiliar with the patients. Each scintigram was graded from 0 to 4+ myocardial uptake, using a modification of the grading system used by Willerson and co-workers, where 2+ represented an intensity equal to that of the ribs and 4+ equaled the intensity of the sternum. Intraobserver variability was encountered only in classifying zero or 1+ scans, which were considered negative.

All statistical analyses were done using analysis of variance with multiple comparisons between group means with the aid of a Sigma 3 computer except in analyzing aortic cross-clamp time for which Student’s t-test was used. Before undergoing operation, each patient agreed to the study and signed an informed consent form approved by the University of California, San Diego, Committee on Investigations Involving Human Subjects.

## Results

**ECG**

Six of the 41 patients (15%) developed persistent new Q waves after coronary artery surgery (table 1). In four of these patients the new Q waves were in the inferior leads (II, III and aV\(_r\)). None of these four patients had documented previous inferior myocardial infarctions and all of them had procedures performed on the right coronary artery. Three had endarterectomies of the right coronary artery in addition to bypass grafting. Another six of the 41 patients (15%) had ST-T wave changes postoperatively suggestive of myocardial ischemia. The remaining 29 patients had either no ECG changes or transient nonspecific ST-T wave abnormalities.

**MB-CPK**

None of the 41 patients had detectable MB-CPK preoperatively. All but four had MB-CPK detected postoperatively. The mean MB-CPK values at each sampling time for groups showing different ECG patterns are illustrated in figure 1. Patients with new persistent Q waves had the highest MB-CPK values, patients with ST-T wave abnormalities exhibited intermediate values, and patients with no or nonspecific ECG changes had the lowest values. The best separation among the three ECG groups occurred at the 12-hour sample: no or nonspecific ECG changes, 8 ± 1 (se) I.U./L; ischemic ST-T wave changes, 18 ± 5 I.U./L, and new Q waves, 60 ± 16 I.U./L.

The MB-CPK area was evaluated for each of the three ECG groups and the mean values are illustrated in figure 2. The mean for the group with no or nonspecific ECG changes was 262 ± 47 I.U./L · hr. The mean value for the group with ischemic ST-T changes was 708 ± 65 I.U./L · hr and the value for the group with persistent new Q waves was 1598 ± 545 I.U./L · hr. Analysis of variance showed a significant difference in mean MB-CPK area between the patients with persistent new Q waves and the other two groups (P < 0.05 overall).
was 465 I.U./L · hr, and this value was considered as the upper limit of normal. The mean value of the patients with no or nonspecific ECG changes was below this value and the mean of the other two groups was above it (fig. 2). All of the patients with ischemic ST-T wave changes or new persistent Q waves had values greater than 465 I.U./L hours. However, six individual patients in the group without significant ECG changes postoperatively had values higher than 465.

Pyrophosphate Scans

Ten of the 41 patients (24%) had a postoperative scan positive for myocardial uptake. Five showed discretely localized uptake, four of whom had new Q waves on ECG which correlated with the site of damage on scan. In the other five patients the uptake was diffuse and all but one had only ischemic ST-T wave changes on ECG. In the 26 patients who had had preoperative scans, no scan was positive. Figure 3 shows an example of a diffusely positive postoperative scan in a 39-year-old man (R. B., table 1) who had a triple bypass procedure and right coronary endarterectomy. His ECG showed the development of new Q waves in the inferior leads associated with ischemic ST-T wave changes in the anterolateral leads and his MB-CPK area was over three times the upper limit of normal found in uncomplicated postoperative patients and was the second highest value observed in these patients. Thus, he probably represents the combination of an inferior transmural myocardial infarction and an anterolateral subendocardial infarction.

Comparison of the Three Techniques (table 1)

The relative sensitivity of the three techniques for detecting myocardial damage is illustrated in figure 4. The upper left hand quadrant represents the ten patients who definitely had myocardial necrosis postoperatively, since they had both positive pyrophosphate scans and MB-CPK levels higher than the upper limit in uncomplicated cases. Five of these ten patients had new postoperative Q waves on ECG and five had ischemic ST-T wave changes. In the lower right hand quadrant are the 23 patients with no evidence by MB-CPK area or scan of postoperative damage. They had no or nonspecific ECG changes. No patient had a positive scan without an elevated CPK, as illustrated in the lower left quadrant. However, eight patients had high MB-CPK values and negative scans as demonstrated in the upper right hand quadrant. One patient had ischemic ST-T wave changes and one developed a new Q wave, but six of these eight patients had no or nonspecific ECG changes. Thus, in the six patients who had no definite evidence of myocardial necrosis by ECG or scan, the elevated CPK values may have been related to the operative procedure itself.

Detection of Myocardial Infarction

Based on these results we developed two sets of criteria for perioperative myocardial damage: 1) new persistent Q waves and either an elevated MB-CPK area or a positive pyrophosphate scan; 2) ischemic ST-T wave changes and both an elevated MB-CPK area and a positive scan. Using these criteria 11 of the 41 patients (27%, numbers 1 through 11 in table 1) demonstrated myocardial damage after surgery. Mean cross-clamp time averaged 27 min in those without evidence of myocardial necrosis as compared to 38 min in those with evidence of necrosis (P < 0.05). However, there was no difference in the preoperative left ventricular ejection fraction, the severity of the coronary artery disease, the number of grafts inserted or the number of endarterectomies performed between the patients who did and those who did not have evidence of perioperative damage.

FIGURE 3. Pre and postoperative pyrophosphate scans, ECGs, and MB-CPK area in a patient who suffered a postoperative myocardial infarction.

FIGURE 4. Comparison of the three noninvasive techniques for detecting myocardial damage after bypass surgery. PYP = pyrophosphate scan.
Discussion

Early experience with coronary artery bypass graft surgery indicated that a significant percentage of patients develop ECG evidence of new transmural infarction in the immediate postoperative period. As more experience was gained, it became apparent that there were certain problems in analysis of the ECG postoperatively in such patients. The ECG has, of course, limitations that are not unique to the postoperative setting such as the inability to diagnose myocardial infarction in the presence of left bundle branch block. More importantly, many patients have severe ST-T wave changes after coronary artery surgery which suggest ischemia, but could be due to pericarditis or metabolic abnormalities. It seems reasonable to suppose that some of these patients have subendocardial infarction, and our results support this hypothesis. All six patients with ischemic ST-T wave changes had an elevated MB-CPK area and five of the six had positive pyrophosphate scans.

The specificity of the Q wave in the postoperative patient after coronary bypass has also been questioned. Transient Q waves that resolve rapidly after the cessation of bypass have been detected intraoperatively during cardiopulmonary bypass. Theoretically, the conditions producing these changes (ischemia, electrolyte imbalance, etc.) could resolve more slowly, giving the false impression of myocardial infarction in the early postoperative period. In our study all new Q waves persisted until hospital discharge. Another report related the appearance of new Q waves in certain patients after successful revascularization of an ischemic anterior wall. These patients had evidence of previous inferior wall myocardial infarction by left ventricular angiography, but not ECG. The authors suggested that the old inferior changes were unmasked by the improved anterior wall function.

These potential limitations do not apply to our series. Although in four of our six patients with new postoperative Q waves the inferior surface was involved, none could be ascribed to unmasking of an old infarction. Also, all of our patients with new Q waves had an elevated MB-CPK area and all but one had a positive pyrophosphate scan. Furthermore, other studies have confirmed the specificity of new Q waves on ECG by repeat left ventricular angiography or in some cases by autopsy studies. Thus, the appearance of persistent new Q waves on ECG after coronary artery bypass graft surgery appears to be highly specific for acute myocardial infarction.

Early studies on serum enzyme release after cardiac surgery demonstrated that almost all patients had rises in CPK, GOT, and LDH, and although the patients with definite myocardial infarction had somewhat higher values, there was no reliable separation point. In more recent studies employing the MB-isoenzyme of CPK, rises in this enzyme in most patients undergoing cardiac surgery have been found, suggesting that elevations in this enzyme may be due to coronary artery surgery per se rather than to myocardial infarction. Most of the patients in our study also had MB-CPK detected after surgery; however, all patients with other evidence of myocardial damage exhibited a greater amount of MB-CPK release than patients with a completely uncomplicated postoperative course. Unfortunately, the separation by MB-CPK was not perfect because six patients had elevated values with no ECG changes and negative pyrophosphate scans. Thus, the MB-CPK determination is useful for confirming the presence of myocardial damage in patients without diagnostic ECG changes, but by itself does not appear specific for myocardial necrosis.

Recently, several studies have advocated the reliability, sensitivity, and specificity of pyrophosphate scanning for detecting myocardial damage after coronary artery surgery; however, both false positive and false negative results can occur. Although we observed no false positive scans in our patients, calcified left ventricular aneurysms or heavily calcified valves have been shown to appear as positive scans. Ideally, preoperative scans should be performed in all patients. One patient in our study had a negative scan postsurgery with an elevated MB-CPK area and a new Q wave on ECG. This patient was scanned the sixth day after surgery. Our most recent experience and that of others suggests that formerly positive scans may become negative (0–1–r) in as early as five days. Therefore, we now obtain scans two to three days after surgery, if possible, in order to obtain maximum intensity.

The incidence of perioperative myocardial damage was increased in our patients from 15%, based on ECG Q waves alone, to 27% utilizing our new criteria as described above. However, the mechanism responsible for perioperative damage was not clear from our study. The only positive correlation was a longer total cross-clamp time in those who demonstrated evidence of perioperative necrosis. This association has been noted by other investigators and some have reported a higher incidence of necrosis in those patients undergoing endarterectomy in addition to bypass grafting. Although three of the six patients who developed new Q waves had right coronary endarterectomy, there was no significant difference in the number of endarterectomies done between those with and without postoperative myocardial damage.

Other factors such as the number of diseased vessels or the number of grafts performed that have been found significant by others were not of predictive value in our patients. Also, it has been reported that MB-CPK appears in the serum of some patients before cardiopulmonary bypass is instituted and postoperatively, suggesting that the induction of anesthesia may be a critical factor involved in perioperative myocardial damage with coronary artery bypass graft surgery. The exact mechanism of myocardial damage may become apparent as further studies are done using a combination of these three noninvasive techniques.

References
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Effects of Operation on Left Atrial Size and the Occurrence of Atrial Fibrillation in Patients with Hypertrophic Subaortic Stenosis

DONALD C. WATSON, M.D., WALTER L. HENRY, M.D., STEPHEN E. EPSTEIN, M.D., AND ANDREW G. MORROW, M.D.

SUMMARY The relation between left atrial size and atrial fibrillation was examined in 37 patients who had left ventriculotomy and myectomy at the National Heart and Lung Institute. Atrial fibrillation was present in 11 of 27 (41%) patients with an echocardiographically measured left atrial dimension greater than 45 mm. No patient with a left atrial dimension less than 45 mm had atrial fibrillation pre or postoperatively. Eleven of 13 patients less than 40 years of age with an abnormal preoperative left atrial dimension had a 10% or greater reduction in left atrial dimension postoperatively. A group of 21 patients 40 years of age or older had an abnormal left atrial dimension preoperatively, and no significant change postoperatively. These results indicate that left ventriculotomy and myectomy can produce a significant decrease in left atrial size in younger patients with idiopathic hypertrophic subaortic stenosis. It is hoped that the decrease in atrial size may reduce the risk of atrial fibrillation in these patients.

In one study, atrial fibrillation, with rare exception, occurred in patients with a dilated left atrium. The present study was undertaken to determine whether there is a similar relation between left atrial size and atrial fibrillation in patients with obstructive ASH (idiopathic hypertrophic subaortic stenosis, IHSS) who have had left ventricular outflow obstruction relieved by myotomy and myectomy. The results of this study are relevant to the controversy concerning the efficacy of operation in this condition. The reduction in left ventricular outflow gradient that occurs following myotomy and myectomy is thought to reflect a favorable hemodynamic change responsible for the symptomatic improvement experienced by most patients. However, other investigators have suggested that abolition of the gradient may be due to the damage that has been inflicted upon the left

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Received June 16, 1976; revision accepted August 16, 1976.
Detection of perioperative myocardial damage after coronary artery bypass graft surgery.

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doi: 10.1161/01.CIR.55.1.173

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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