Anesthesiology
1997; 86:576–91

Electrocardiographic and Hemodynamic Changes and Their Association with Myocardial Infarction during Coronary Artery Bypass Surgery

A Multicenter Study

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Background: **Electrocardiographic (ECG) changes during coronary artery bypass graft surgery have not been described in detail in a large multicenter population. The authors describe these ECG changes and evaluate them, along with demographic and clinical characteristics and intraoperative hemodynamic alterations, as predictors of myocardial infarction (MI) as defined by two sets of criteria.**

Methods: **Data from 566 patients at 20 clinical sites, collected as part of a clinical trial to evaluate the efficacy of acadesine for reducing MI, were analyzed at core laboratories. Perioperative ECG changes were identified using continuous three-lead Holter ECG. Systolic blood pressure, diastolic blood pressure, and heart rate were recorded each minute during operation. The occurrence of MI by Q wave or myocardial fraction of creatine kinase (CK-MB) or autopsy criteria, and by (Q wave and CK-MB) or autopsy criteria was determined.**

Results: **During perioperative Holter monitoring, episodes of ST segment deviation, major cardiac conduction changes ≥30 min, or use of ventricular pacing ≥30 min occurred in 58% patients, primarily in the first 8 h after release of aortic occlusion. Of the 25% patients who met the Q wave or CK-MB or autopsy criteria for MI, 19% had increased CK-MB as well as ECG changes. (Q wave and CK-MB) or autopsy criteria for MI were met by 4% of patients. The CK-MB concentration generally peaked by 16 h after release of aortic occlusion. In patients with (n = 187) and without a perioperative episode of ST segment deviation, the incidence of MI was 36% and 19%, respectively (*P* < 0.01), by Q wave or CK-MB or autopsy criteria, and 6% and 3%, respectively (*P* = 0.055), by (Q wave and CK-MB) or autopsy criteria. Multiple logistic regression analysis showed that intraoperative ST segment deviation, intraventricular conduction defect, left bundle branch block, duration of hypotension (systolic blood pressure < 90 mmHg) after cardiopulmonary bypass, and duration of cardiopulmonary bypass are independent predictors of Q wave or CK-MB or autopsy MI. The independent predictors of (Q wave and CK-MB) or autopsy MI are intraoperative ST segment deviation and duration of aortic occlusion.**

Conclusions: **Major ECG changes occurred in 58% of patients during coronary artery bypass graft surgery, primarily within 8 h after release of aortic occlusion. Multicenter data collection revealed a substantial variation in the incidence of MI and an overall incidence of up to 25%, with most MI occurring within**

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Received from the Departments of Anesthesia at the University of California, San Francisco, California; University of Montreal, Montreal, Quebec; Medical College of Wisconsin, Milwaukee, Wisconsin; Emory University, Atlanta, Georgia; Harvard Medical School, Boston, Massachusetts; the Ischemia Research and Education Foundation (IREF), San Francisco, California; the Department of Medicine, University of California, San Francisco, and the institutions of the *McSPI* Research Group. Submitted for publication June 12, 1996. Accepted for publication November 21, 1996. Supported in part by the Ischemia Research and Education Foundation and Gensia Pharmaceuticals, Inc. Presented in part at the annual meeting of the American Society of Anesthesiologists, San Francisco, California, October 15–19, 1994.

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16 h after release of aortic occlusion. Intraoperative monitoring of ECG and hemodynamics has incremental value for predicting MI. (Key words: Anesthesia: cardiac; risk factors. Anesthetic, intravenous: fentanyl. Complications: bradycardia; hypertension; hypotension; myocardial infarction; myocardial ischemia; tachycardia. Enzymes, cardiac-specific: CK-MB. Heart: conduction; ejection fraction; heart rate; infarction; ischemia; pacing. Monitoring: blood pressure; electrocardiography; hemodynamics; Holter electrocardiography. Surgery: cardiac; coronary artery bypass graft.)

MYOCARDIAL ischemia is prevalent in patients undergoing coronary artery bypass graft (CABG) surgery.[1-7] Although electrocardiography (ECG) is commonly used to monitor for myocardial ischemia,[1-7] the changes observed in the ECG have not been described in detail in a large multicenter population. This is especially true of changes other than ST segment depression. Development of a significant Q wave detected by 12-lead ECG and increased myocardial fraction of creatine kinase (CK-MB) are the most commonly used indicators of perioperative myocardial infarction (MI), although there are no widely accepted criteria for MI.[1-7] The timing of occurrence of ischemia and MI has not been described in detail.

Demographic and clinical characteristics[8] and intraoperative ECG changes[1,2,4,6] are reported to be associated with MI and other measures of outcome. Establishment of the incremental value of intraoperative ECG changes and hemodynamic abnormalities for the prediction of MI would help researchers develop strategies to reduce the incidence of MI.

Our objective was to study the various types of perioperative ECG changes and to determine their association with MI, changes in CK-MB, and left ventricular ejection fraction (EF). Multiple logistic regression was used to determine the independent predictive value of preoperative or intraoperative demographic, clinical, Holter ECG and hemodynamic variables for MI as defined by two sets of criteria.

Materials and Methods

Study Population

Data were collected from 633 patients undergoing CABG surgery between June 1991 and April 1992 at 20 clinical sites (members of the Multicenter Study of Perioperative Ischemia [*McSPI*] Research Group; see Appendix 1), as part of a randomized clinical trial (trial 1016) evaluating the effect of acadesine on the incidence of perioperative MI.[5] Results are presented for 566 patients for whom Holter ECG data were available.

Included were patients older than 35 yr who had ≥50% stenosis of the left main coronary artery, ≥70% stenosis of at least two major coronary arteries, or both. Excluded were patients with valvular disease, MI within 7 days before surgery, cardiogenic shock, renal or hepatic insufficiency, patients whose ECG could not be interpreted for ST segment deviation due to preoperative ventricular pacing or left bundle branch block (LBBB), and patients in whom esophageal disease precluded placement of a transesophageal echocardiographic probe. Institutional approval and written informed consent were obtained. For 7 h beginning 15 min before induction of anesthesia, placebo was administered to 187 patients; 0.05 $mg \cdot kg^{-1} \cdot min^{-1}$ acadesine was given to 192 patients; and 0.1 $mg \cdot kg^{-1} \cdot min^{-1}$ acadesine was given to 187 patients.

Perioperative Course

As described previously, patients were premedicated with 1–4 mg lorazepam given orally.[5] Preoperative cardiovascular medications were continued until surgery. Anesthesia was provided using fentanyl, supplemented by midazolam and thiopental.[5] Vecuronium was used to achieve muscle relaxation. Standard monitoring was used. Anti-ischemic medications (such as nitrates and calcium channel blockers) were not administered prophylactically. Postoperative analgesia and sedation were provided with morphine sulfate and midazolam. The trachea was usually extubated on the morning after surgery.

Holter Electrocardiography

Continuous three-channel Holter (series 8500, Marquette Electronics, Milwaukee, WI) ECG monitoring was performed in all 566 patients for at least 8 h before surgery until 48 h after the start of surgery. Bipolar ECG leads, modified CM_5, CC_5, and modified ML were recorded. Modified CM_5 from the left shoulder to V_5 recorded the anterior forces. CC_5 from right-sided V_5 to left-sided V_5 recorded anterior and lateral forces. Modified ML from the left shoulder to the center of the left anterior and posterior iliac spines recorded the inferior forces. After placement of the Holter monitor before operation, the ECG was recorded in the supine, left lateral decubitus, right lateral decubitus, and sitting positions to quantify the effect of body position changes on ST segment deviation.

At the core laboratory, the Holter ECG processing by one investigator (level 1) using a Marquette SXP Laser Holter scanner was verified by two additional investigators (levels 2 and 3). The duration of monitoring was divided into the following periods: preoperative period, from the onset of monitoring to the start of induction of anesthesia; pre-CPB period, from the start of induction of anesthesia to the onset of CPB; CPB period, from the onset to the end of CPB; post-CPB period, from the end of CPB to chest closure; and postoperative period, from chest closure to discontinuation of monitoring. The CPB period included durations when QRS complexes were present before and after asystole due to cardioplegic arrest. To evaluate the univariate and multivariable association with MI, a patient was considered to have intraoperative ST segment deviation if at least one episode of ST segment deviation started or ended during the period between induction of anesthesia and chest closure.

Holter Electrocardiographic Changes. Of the many changes observed in Holter ECG, the following were studied. The ECG was considered uninterpretable for detecting ST segment deviation indicative of ischemia during ventricular pacing, LBBB and intraventricular conduction defect, and the presence of a superior QRS axis (*i.e.*, an rS pattern in all the monitored leads). Excessive noise also could render the ECG uninterpretable. The QRS complex was considered to be small if the total QRS amplitude in the lead with the largest QRS complex was less than 5 mm. The duration of these changes and of right bundle branch block (RBBB) was determined.

ST segment deviation usually was measured 60 ms after the J point. In the presence of left ventricular hypertrophy with strain pattern or atrial fibrillation, ST segment deviation was measured at the J point. ST segment deviation considered to be due to change in body position, hypothermia, defibrillation, transient cardiac conduction change, or pericarditis was excluded.[1,2] Episodes of ST segment deviation were identified by reviewing the ECG complexes as previously described.[1,5,9]

The duration of each episode was defined by the time from which the ST segment deviated from the local baseline value to the time when the ST segment reverted to a steady-state value in the ECG lead with the largest peak ST segment deviation. Local baseline was defined as the steady-state period usually less than 15 min before the episode. Episodes lasting at least 1 min and of at least 1-mm peak ST segment deviation from the local baseline were retained. Episodes were considered discrete if they occurred at least 1 min apart. Characteristics recorded for each episode of ST segment deviation were the time of onset, duration, peak ST segment deviation from the local baseline, heart rate (HR) during the local baseline, and HR at the onset of ST segment deviation. Each episode was assigned to the lead with the greatest peak ST segment deviation, even when the deviation exceeded 1 mm in two or three leads.

For each ischemic episode, the ST segment deviation amplitude-duration integral (area under the curve [AUC]) was calculated. To determine the incidence of ischemic ST segment deviation, an episode of ST segment deviation starting in one perioperative period and ending in another was assigned to the period in which it began. The duration and AUC of ST segment deviation in each period was assigned to that period.

Hemodynamics

We determined preoperative baseline values for systolic blood pressure (SBP), diastolic blood pressure (DBP), and HR by averaging three values obtained noninvasively when the patient was at rest in the hospital. During operation, HR and invasive SBP and DBP were recorded every minute using ARKIVE (Diatek, San Diego, CA) and the monitoring equipment at the clinical site. As per protocol,[5] during the pre-CPB period, SBP and HR were to be maintained within 20% of preoperative baseline values by adjusting the depth of anesthesia and administering fluids and cardiovascular medications. During CPB, SBP was to be maintained between 40 and 80 mmHg; during the post-CPB period, SBP was to be maintained between 90 and 130 mmHg, with HR at $<$ 110 beats/min.[5]

The association between the occurrence of MI and the number of per-minute samples of SBP, DBP, and HR that crossed a wide range of thresholds in the pre-CPB or post-CPB periods was determined. Results are presented for the protocol-specified thresholds.[5] We also noted the range of thresholds for which an association was present.

Detection of Myocardial Infarction

Myocardial infarction was defined as fulfilling the Q wave or CK-MB or autopsy criteria listed below. A more conservative definition of MI as fulfilling (Q wave and CK-MB) or autopsy criteria also was used.

12-Lead Electrocardiography. We obtained a standard 12-lead ECG before surgery, immediately after surgery, on the mornings of postoperative days (POD) 1, 2, 3, and 5, and at hospital discharge. At the core laboratory (Appendix 2), each ECG was first analyzed using the Minnesota Code criteria.[10] The occurrence of Q wave code 1.1 to 1.3 (except 1.2.8) was determined in one or more of the three lead groups: anterolateral (I, AVL, V_6), posterior-inferior (II, III, AVF), and anterior (V_1-V_5). After coding, two physician-electrocardiographers independently evaluated the complete set of ECG for each patient to determine if Q wave criteria for the development of a perioperative MI were met in one or more of the three lead groups. If the two electrocardiographers disagreed, the evaluation of a third electrocardiographer was accepted.

CK-MB. We obtained serum samples for analysis of CK-MB, before operation and at 1, 4, 8, 12, 16, 20, 24, 28, 32, 36, 42, 48, and 60 h after the release of aortic occlusion. At the core laboratory (Appendix 2), CK-MB concentration was measured by an immunoenzymetric assay (Tandem-E CK-MB II, Hybritech Diagnostics, La Jolla, CA). To detect MI, the CK-MB thresholds were defined as ≥100 ng/ml in any postoperative sample, or ≥70 ng/ml more than 12 h after release of aortic occlusion, or ≥12 ng/ml more than 24 h after release of aortic occlusion.[5]

Autopsy Myocardial Infarction. Standard criteria for MI were used during autopsy performed at the clinical site.

Ventriculography

Preoperative EF was determined at the clinical site from cardiac catheterization performed within 6 months before surgery.[5] Postoperative EF was determined at the clinical site from radionuclide ventriculography performed within 14 days after surgery.

Transesophageal Echocardiography

The results of transesophageal echocardiographic analysis have been presented in part elsewhere[5] and are not described here.

Statistical Analysis

The statistical software used was SAS version 6.09 on the Unix platform (SAS Institute, Cary, NC). The Cochran-Mantel-Haenszel test was used to determine the effect of acadesine on the association of MI with ST segment deviation. For dichotomous variables, we used the chi-squared test or Fisher's exact test. For variables with skewed distributions, the Wilcoxon rank sum test was used. Two-tailed $P < 0.05$ was considered significant.

To determine the incremental value of Holter ECG and hemodynamic variables to predict MI, univariate and multivariable models of association with MI were constructed for these variables, the use of acadesine, and the clinical and demographic variables previously reported[1,2,4,6,8] to be predictors of MI. Univariate predictors of MI with nominal two-tailed $P \le 0.2$ were identified using the chi-squared test or Fisher's exact test for dichotomous predictors, and logistic regression for categorical and continuous predictors. The logistic models were based on predictors having a probability value of 0.10 or less. Odds ratio and 95% confidence interval based on standard error of the logistic coefficient and two-tailed probability value are presented.

The multivariable models were selected to optimize discrimination (the ability to separate MI from non-MI) and calibration (the difference between observed and estimated incidence of MI). A larger area under the receiver-operating characteristic curve signifies better discrimination.[11,12] Greater value of the Hosmer-Lemeshow goodness-of-fit statistic and a probability value greater than 0.05 are associated with better calibration.[12,13]

Results

Demographic and Clinical Characteristics

Table 1 shows the demographic and clinical characteristics of the 566 patients.

Effect of Acadesine

Acadesine did not have a significant effect on the occurrence of ST segment deviation and its association with MI. No episodes of ST segment deviation, at least one episode of ST segment depression, and at least one episode of ST segment elevation occurred in 68%, 25%, and 11%, respectively, of patients in the placebo group; 64%, 29%, and 13% of patients in the low-dose acadesine group; and 70%, 19%, and 15% of patients in the high-dose acadesine group. The percentages of patients who met Q wave or CK-MB or autopsy criteria, Q wave criteria, and CK-MB criteria for MI were 25%, 8%, and 22%, respectively, in the placebo group; 28%, 9%, and 23% in the low-dose acadesine group; and 21%, 6%, and 18% in the high-dose acadesine group. Because the differences among the three groups were not significant for

Table 1. The Number and Percentage of Patients with Various Preoperative and Intraoperative Characteristics or the Values of Those Characteristics (n = 566)

Characteristics	No. (%) or Value
Preoperative characteristics	
Mean age (yr)	63 ± 9
Age > 65 yr	239 (42)
Female gender	108 (19)
History of unstable angina	222 (40)
History of hypertension	338 (60)
Previous myocardial infarction	284 (50)
History of congestive heart failure	63 (11)
Previous coronary artery bypass graft surgery	55 (10)
Previous coronary angioplasty	78 (14)
Preoperative hematocrit (%)	34 ± 3
Cardiac catheterization	
Left main coronary stenosis ≥ 50%	125 (22)
Preoperative ejection fraction (n = 408)	
≤ 40%	76 (13)
≤ 30%	23 (6)
Left ventricular end-diastolic pressure (mmHg) (n = 439)	17 ± 7
Intraoperative characteristics	
Aortic occlusion duration (min)	57.4 ± 21.8
Cardiopulmonary bypass duration (min)	104.4 ± 35.6
Mean number of grafts	3.3 ± 0.9
Patients receiving internal mammary artery graft	497 (81)
Non-blood cardioplegia	182 (32)
Blood cardioplegia	384 (68)
Surgeon's assessment of revascularization	
Poor	5 (1)
Fair	35 (6)
Good or exellent	526 (93)

Values are mean ± SD.

these parameters, we combined the groups for the following analyses.

Holter Electrocardiographic Changes

For the 566 patients studied, we recorded 31,715 h of continuous Holter ECG data.

Incidence of Holter Electrocardiographic Changes. Every patient had a change in Holter ECG during perioperative monitoring. The numbers of patients with changes considered to be major are presented in table 2. At least one episode of ST segment deviation, cardiac conduction change (≥30 min), or ventricular pacing (≥30 min) (table 2) occurred in 58% of 566 patients. There were 322 episodes of ST segment depression; that is, a mean of 2.4 episodes in 24% of patients. There were 104 episodes of ST segment elevation; that is, a mean of 1.4 episodes in 13% of patients. At least one episode of ST segment deviation occurred in 33% of patients and at least one episode each of ST segment elevation and depression in 4% of patients. In leads CM_5, CC_5, and ML, maximum ST segment depression occurred in 57%, 39%, and 4% of episodes, respectively, and maximum ST segment elevation occurred in 44%, 9%, and 47% of episodes.

Temporal Pattern of Holter Electrocardiographic Changes. Figure 1 shows the time courses of ST segment deviation, new small QRS complex, RBBB, ventricular pacing, superior QRS axis, intraventricular conduction defect, and LBBB. Table 3 shows the number of patients with ST segment deviation in the various perioperative periods.

In the pre-CPB period, of the five episodes of ST segment elevation, three occurred in three patients undergoing repeated operation for CABG, one of whom met CK-MB criteria for MI, and another met CK-MB and inferior Q wave criteria for MI. During CPB, before asystole, there were eight episodes of ST segment elevation and no episodes of ST segment depression. During CPB, after release of aortic occlusion, there were 37 episodes of ST segment elevation and ten episodes of ST segment depression. After release of aortic occlusion, the pattern of cardiac conduction change varied over time and often was different than the standard patterns of persistent conduction change, such as LBBB.

Characteristics of ST Segment Deviation. Figure 2 shows the characteristics of ST segment deviation in each perioperative period. ST segment deviation was greater for episodes of elevation than for depression (2.5 ± 1.6 mm *vs.* 1.5 ± 0.6 mm; $P < 0.05$). In patients who met Q wave criteria for MI, HR at the onset of episodes of ST segment deviation was less than baseline HR by 11.5 ± 33.3 beats/min in the CPB period and by 11.5 ± 9.9 beats/min in the post-CPB period.

Hemodynamics

We recorded 1,560 h of continuous SBP, DBP, and HR data from 318 patients. The time-averaged values of SBP, DBP, and HR were 123 ± 13 mmHg, 62 ± 8 mmHg, and 59 ± 10 beats/min, respectively, in the pre-CPB period, and 107 ± 11 mmHg, 58 ± 7 mmHg, and 86 ± 11 beats/min, in the post-CPB period. In the post-CPB period, there were ten or fewer per-minute samples of

Table 2. CK-MB, Q Wave, and Change in EF in Patients with Various ECG Changes during Perioperative Monitoring (n = 566).

Category	No. of Patients	Peak CK-MB (ng/ml)	% Patients with Peak CK-MB by 16 h	MI by CK-MB (%)	MI by Q wave (%)	Postop EF% −Preop EF% (n = 333)
No abnormality	114	41 ± 18	93	0	0	1.9 ± 10.5
Only small QRS	105	45 ± 29	92	0	0	1.7 ± 10.7
Cardiac conduction changes						
Only RBBB	92	43 ± 31	95	0	0	2.0 ± 13.1
Superior QRS axis	82	75 ± 65*	92	27	10	1.6 ± 13.7
IVCD	58	92 ± 92*	86	25	9	−3.2 ± 16.2
LBBB	24	87 ± 67*	79	35	8	−4.9 ± 16.5*
Only pacing	17	39 ± 14	71	0	0	0.2 ± 13.8
ST segment deviation						
ST ↓ CM_5, CC_5	129	81 ± 91*	81	31	9	−0.6 ± 13.8
ST ↓ ML	8	79 ± 90*	75	25	0	5.6 ± 8.1
1–1.9 mm ST ↓	119	75 ± 79*	80	28	8	−0.9 ± 13.6
≥2 mm ST ↓	41	101 ± 112*	83	37	7	4.6 ± 12.5
ST ↑ CM_5, CC_5	45	104 ± 102*	80	35	18	−1.6 ± 12.9
ST ↑ ML	27	118 ± 128*	82	41	30	−4.0 ± 13.3
1–1.9 mm ST ↑	25	118 ± 97*	76	48	28	−3.3 ± 13.1
≥ 2 mm ST ↑	54	109 ± 115*	82	37	19	−3.2 ± 12.8
Myocardial infarction (12 − lead ECG)						
Anterior Q wave	11	119 ± 130*	73	33	100	−6.9 ± 8.5*
Anterolateral Q wave	9	158 ± 141*	78	56	100	−10.2 ± 16.8*
Inferior Q wave	36	131 ± 115*	72	49	100	−2.5 ± 10.8
CK-MB	116	173 ± 104*	66	100	17	−3.8 ± 15.4

Values are mean ± SD.

MI = myocardial infarction; EF = left ventricular ejection fraction; No abnormality = none of the listed ECG changes except small QRS (< 5 mm); Only small QRS = small QRS complex ≥ 30 min and no other listed ECG changes; Only RBBB = right bundle branch block ≥ 30 min and no other listed ECG changes except small QRS; IVCD = intraventricular conduction defect ≥ 30 min; LBBB = left bundle branch block ≥ 30 min; Only pacing = ventricular pacing ≥ 30 min and no other listed ECG changes except small QRS; CM_5, CC_5 = Holter leads CM_5 or CC_5; ML = Holter lead ML; ST↓ = ST segment depression episode; ST↑ = ST segment elevation episode.

* $P \leq 0.05$ *versus* the "no abnormality" group.

SBP < 90 mmHg in 60% of patients and no per-minute samples of HR > 110 beats/min in 86% of patients. None of the hemodynamic changes evaluated was significantly associated with intraoperative ST segment deviation.

Myocardial Infarction

A total of 3,798 12-lead ECGs and 6,777 CK-MB samples were analyzed. Of the 25% patients who met Q wave or CK-MB or autopsy criteria for MI, 19% (of 566) met CK-MB criteria and had a major ECG change (Q wave, ST segment deviation, cardiac conduction changes, or ventricular pacing; see table 2), or met Q wave criteria and had peak CK-MB values greater than 59 ng/ml (mean + SD of the peak CK-MB value in patients in the No Abnormality category in table 2). The greatest incidence of Q wave or CK-MB or autopsy MI at a single clinical site was 50% (n = 14); the lowest incidences were 0% (n = 3) and 8% (n = 12). The incidence (31%) at the ten clinical sites (n = 342) with the greatest incidence was greater ($P < 0.01$) than the incidence (15%) at the remaining ten sites (n = 224). (Q wave and CK-MB) or autopsy criteria for MI were met by 4% of the patients.

All patients who met autopsy criteria for MI also met CK-MB criteria. Of the patients who met Q wave criteria for MI, 46% also met CK-MB criteria, whereas only 17% of the patients who met CK-MB criteria also met Q wave criteria. Of the 116 patients who met the CK-MB criteria for MI, 85% met the ≥100 ng/ml criterion, 12% met the ≥70 ng/ml criterion, and 3% met the ≥12 ng/ml criterion.

Q wave was first observed immediately after surgery in 41% of patients, on POD 1 in 39%, on POD 2 in 11%,

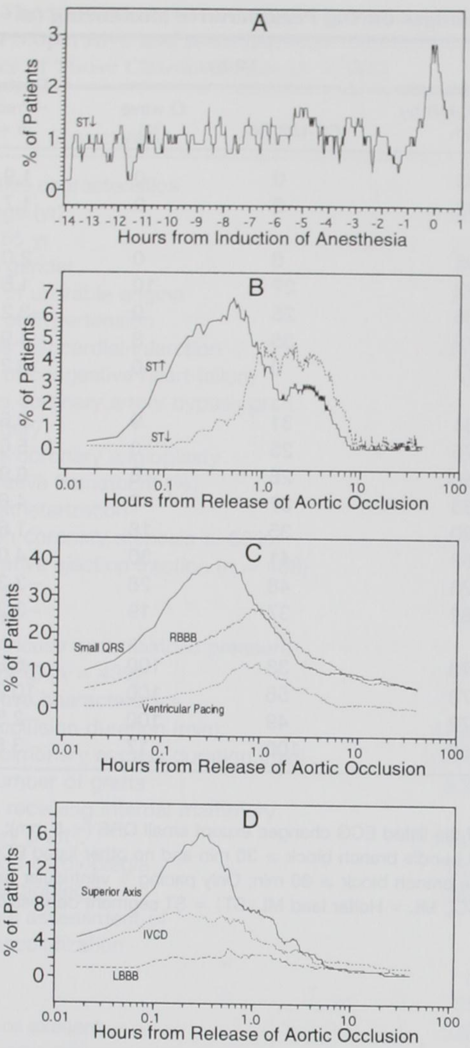

Fig. 1. As a function of time, the percentage of patients whose Holter electrocardiographic data were interpretable for ST segment deviation and who had (*A*) ST segment depression (ST↓) before aortic occlusion or (*B*) ST segment depression (ST↓) or ST segment elevation (ST↑) after release of aortic occlusion. As a function of time after release of aortic occlusion, the percentage of all patients with (*C*) small QRS complex (<5 mm), right bundle branch block (RBBB), ventricular pacing, or (*D*) superior QRS axis, intraventricular conduction defect (IVCD), and left bundle branch block (LBBB). Only ST segment depression was prevalent in the preoperative and pre-CPB periods and is presented.

on POD 3 in 5%, and on POD 5 and 6 in 2% each of 44 patients meeting Q wave criteria. Eight hours after release of aortic occlusion, 10.8% of all 566 patients had CK-MB ≥100 ng/ml, gradually decreasing to 9.3% of patients at 24 h.

Ejection Fraction

Preoperative EF values were obtained in 408 patients. Preoperative and postoperative EF values were obtained in 333 patients. Preoperative EF was not associated with MI or Holter ECG abnormalities listed in table 2. Perioperative changes in EF for patients with various ECG changes are listed in table 2.

Association of Electrocardiographic Changes with Various Outcomes

In patients with and without ST segment deviation, 36% and 19% of patients, respectively ($P < 0.01$), met the Q wave or CK-MB or autopsy criteria for MI, and 6% and 3% of patients ($P = 0.055$) met the Q wave and CK-MB or autopsy criteria. Of the 140 patients who met Q wave or CK-MB or autopsy criteria, 49% had at least one episode of ST segment deviation. Of the 21 patients who met (Q wave and CK-MB) or autopsy criteria, 52% had at least one episode of ST segment deviation.

Table 2 presents the association of ECG abnormalities with measures of outcome. A patient with multiple abnormalities was included in each relevant category. In the No Abnormality group, the maximum peak CK-MB value was 89 ng/ml, and the greatest mean CK-MB value was observed 1 h after release of aortic occlusion, although CK-MB values had peaked in only 9 of 566 patients.

Electrocardiographic Lead Groups. The number of episodes of ST segment depression and elevation with maximum deviation in leads CM_5 or CC_5 for patients fulfilling anterior Q wave criteria for MI were 5 and 4, respectively, and, for anterolateral Q wave criteria, 0 and 2. The corresponding numbers for lead ML for patients fulfilling inferior Q wave criteria for MI were 0 and 8, respectively. For the anterior, anterolateral, and inferior Q wave MI groups, medians of peak CK-MB values were 61 ng/ml, 110 ng/ml, and 88 ng/ml, respectively, and 3, 1, and 12 patients had peak CK-MB values less than 59 ng/ml (mean ± SD of the peak CK-MB value in patients in the No Abnormality category in table 2).

Different Perioperative Periods. Peak CK-MB values for the 76 patients with preoperative ST segment deviation were 74 ± 86 ng/ml, which did not differ significantly from 70 ± 72 ng/ml for the remaining 490 patients. During CPB or post-CPB periods, ST segment deviation was more likely to be associated with MI (table 3).

Duration of Electrocardiographic Changes. A

Table 3. The Number of Patients with ST Segment Deviation during the Various Perioperative Periods and the Percentage of Patients Who Met Various Criteria for Myocardial Infarction

		All Periods	Preoperative	Pre-CPB	CPB	Post-CPB	Postoperative
No ST segment deviation	No. of patients	379	490	537	516	519	505
	Q wave or CK-MB or autopsy MI(%)	19	25	24	23	22	23
	Q wave (%)	6	8	7	6	7	8
	MI by CK-MB(%)	16	20	20	20	18	19
ST segment depression	No. of patients	137	75	25	10	31	47
	Q wave or CK-MB or autopsy MI(%)	34*	24	40*	70*	39*	36*
	Q wave (%)	8	7	12	30*	10	4
	MI by CK-MB(%)	30*	23	35*	60*	37*	34*
ST segment elevation	No. of patients	72	3	5	43	16	16
	Q wave or CK-MB or autopsy MI(%)	47*	67*	40	44*	75*	44*
	Q wave (%)	22*	0	20	26*	25*	19
	MI by CK-MB(%)	37*	67*	40	29*	69*	38
ST segment depression or elevation	No. of patients	187	76	29	50	47	61
	Q wave or CK-MB or autopsy MI(%)	36*	25	41*	46*	51*	38*
	Q wave (%)	11*	7	14	26*	15	8
	MI by CK-MB(%)	32*	24	37*	33*	48*	34*

CPB = cardiopulmonary bypass; MI = myocardial infarction.

* $P \leq 0.05$ *versus* the group with no ST segment deviation in the same period.

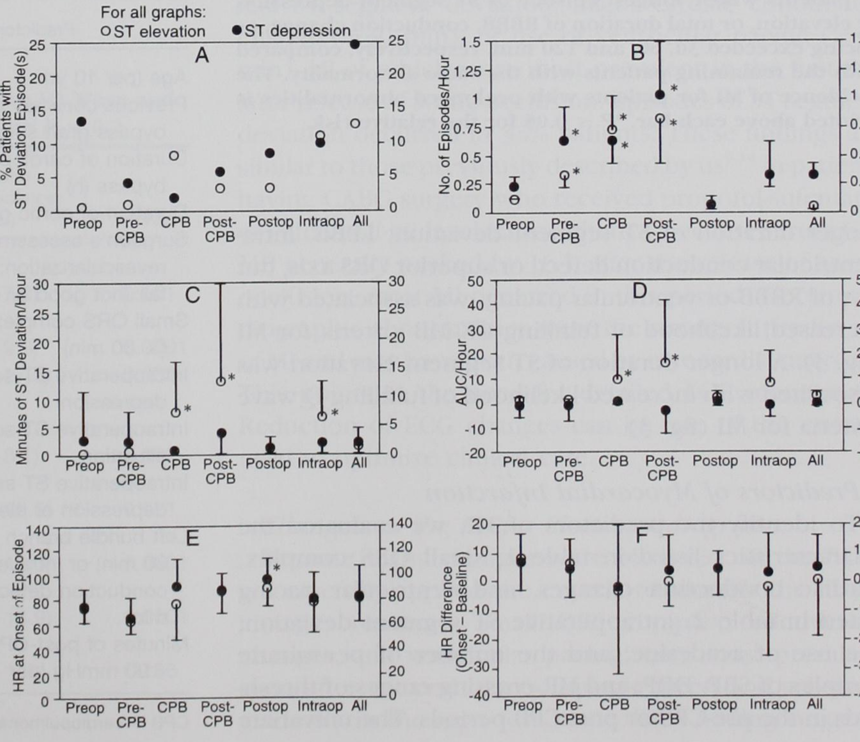

Fig. 2. The parameters of ST segment deviation on Holter electrocardiographic data for preoperative (Preop), pre-cardiopulmonary bypass (Pre-CPB), CPB, post-CPB, postoperative (Postop), total intraoperative (Intraop), and all combined (All) periods are presented. The percentages or means ± SD of each parameter are presented separately for ST segment depression (ST↓) and ST segment elevation (ST↑) episodes. Sometimes the means for the two groups are so close that their graphic displays overlap. *A* and *B* present data for episodes starting in the respective periods. *B* to *D* present means ± SD per hour of interpretable data for each perioperative period only for patients who had ST segment deviation in that period. AUC = area under the curve, i.e., ST segment deviation-duration integral (mm · min); HR = heart rate (beats/min). *$P \leq 0.05$ with respect to the preoperative ST segment deviation of the same type (depression or elevation).

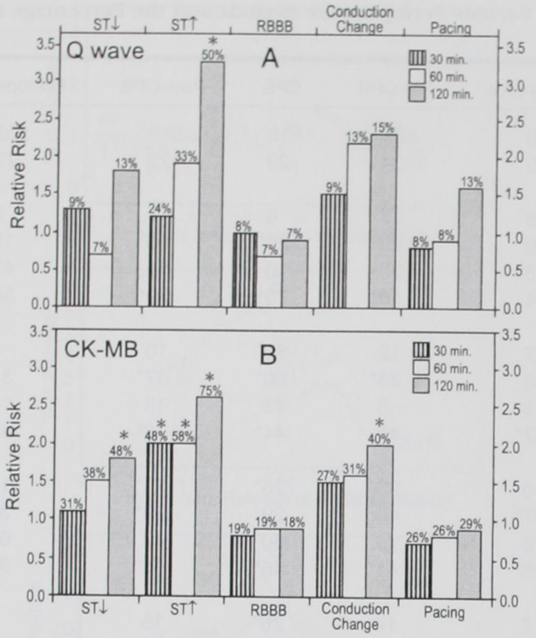

Fig. 3. Data for patients who met (*A*) Q wave criteria for myocardial infarction (MI) or (*B*) CK-MB criteria for MI among patients with ST segment depression (ST↓), ST segment elevation (ST↑), right bundle branch block (RBBB), major cardiac conduction change (*i.e.*, left bundle branch block, intraventricular conduction defect, or superior QRS axis) ≥30 min, or ventricular pacing ≥30 min. The height of the three bars in each of these ten categories represents the relative risk of MI in patients whose longest episode of ST segment depression or elevation, or total duration of RBBB, conduction change, or pacing exceeded 30, 60, and 120 min, respectively, compared with the remaining patients with the same abnormality. The incidence of MI for patients with prolonged abnormalities is printed above each bar. *$P \leq 0.05$ for the relative risk.

longer duration of ST segment deviation, LBBB, intraventricular conduction defect, or superior QRS axis, but not of RBBB or ventricular pacing, was associated with increased likelihood of fulfilling CK-MB criteria for MI (fig. 3). A longer duration of ST segment elevation was associated with increased likelihood of fulfilling Q wave criteria for MI (fig. 3).

Predictors of Myocardial Infarction

To identify the predictors of MI, we evaluated the characteristics listed in table 1; small QRS complex, cardiac conduction changes, and ventricular pacing listed in table 2; intraoperative ST segment deviation; the use of acadesine; and the number of per-minute samples of SBP, DBP, and HR crossing ranges of thresholds in the pre-CPB or post-CPB periods. The univariate predictors of Q wave or CK-MB or autopsy MI with $P \leq 0.2$ are presented in table 4. In addition, the number of per-minute samples of post-CPB HR exceeding any threshold in the range 105% to 170% of the preoperative baseline HR, and the number of per-minute samples of post-CPB SBP less than any threshold in the range 100% to 70% of the preoperative baseline SBP, have univariate association with Q wave or CK-MB or autopsy MI at $P < 0.05$. The numbers of per-minute samples of post-CPB HR and SBP crossing parts of these ranges are independent multivariable predictors of Q wave or CK-MB or autopsy MI. ST segment elevation is the only significant ($P < 0.01$) univariate predictor of the development of a new significant Q wave.

The selected multivariable models of association with Q wave or CK-MB or autopsy MI are presented in table 5. For the model for all 566 patients, the area under the receiver-operating characteristic curve is 0.66 and the goodness of fit is 3.4 ($P = 0.91$). Because the probability value exceeds 0.05, the model has good calibra-

Table 4. Univariate Models of Association with Q Wave or CK-MB or Autopsy Myocardial Infarction with $P \leq 0.2$

Predictor	Odds Ratio (95% Confidence Interval)	*P* Value
Age (per 10 yr)	1.6 (0.9–1.5)	0.111
Previous coronary artery bypass graft surgery	1.6 (0.9–2.8)	0.151
Duration of cardiopulmonary bypass (h)	1.6 (1.2–2.2)	0.002
Duration of aortic occlusion (h)	1.6 (0.9–2.6)	0.091
Surgeon's assessment of revascularization: poor or fair (not good or excellent)	2.4 (1.3–4.7)	0.009
Small QRS complex (< 5 mm) (≥ 30 min)	1.3 (0.9–1.9)	0.192
Intraoperative ST segment depression	2.8 (1.5–5.2)	0.001
Intraoperative ST segment elevation	3.7 (2.1–6.5)	0.0001
Intraoperative ST segment depression or elevation	3.5 (2.2–5.7)	0.0001
Left bundle branch block (≥ 30 min) or intraventricular conduction defect (≥ 30 min)	2.1 (1.3–3.5)	0.004
Minutes of post-CPB SBP <90 mmHg (per 10 min)	1.2 (1.1–1.3)	0.045

CPB = cardiopulmonary bypass; SBP = systolic blood pressure.

Table 5. Multivariable Models of Association with Q Wave or CK-MB or Autopsy Myocardial Infarction

Predictor	Odds Ratio (95% CI)	Coefficient	Standard Error	*P* Value
Not including hemodynamics (n = 566)				
Intraoperative ST segment elevation	4.2 (2.4–7.6)	1.44	0.30	0.0001
Intraoperative ST segment depression	2.8 (1.5–5.4)	1.03	0.33	0.002
Left bundle branch block (≥30 min) or intraventricular conduction defect (≥30 min)	2.3 (1.3–3.9)	0.83	0.28	0.003
Duration of cardiopulmonary bypass (h)	1.6 (1.1–2.2)	0.44	0.17	0.008
Constant		−2.30	0.32	
Including hemodynamics (n = 318)				
Intraoperative ST segment depression or elevation, or intraventricular conduction defect (≥ 30 min), or left bundle branch block (≥ 30 min)	2.1 (1.2–3.7)	0.75	0.29	0.01
Minutes of post-CPB SBP <90 mmHg (per 10 min)	1.2 (1.0–1.3)	0.12	0.06	0.04
Constant		−1.56	0.19	

CI = confidence interval; CPB = cardiopulmonary bypass; SBP = systolic blood pressure.

tion. For the model for 318 patients with hemodynamic data, using the protocol-specified[5] threshold for post-CPB hypotension (SBP $<$ 90 mmHg), the area under the receiver-operating characteristic curve is 0.62 and the goodness of fit is 11.2 ($P = 0.19$).

For (Q wave and CK-MB) or autopsy MI, the univariate predictors with $P \leq 0.2$ are presented in table 6 and the multivariable model of association for all 566 patients is presented in table 7. For this model, the area under the receiver-operating characteristic curve is 0.78 and the goodness of fit is 4.8 ($P = 0.78$).

Table 6. Univariate Models of Association with (Q Wave and CK-MB) or Autopsy Myocardial Infarction with *P* ≤ 0.2

Predictor	Odds Ratio (95% Confidence Interval)	*P* Value
Previous coronary artery bypass graft surgery	2.3 (0.7–7.0)	0.151
Duration of cardiopulmonary bypass (h)	4.6 (2.2–9.6)	0.0001
Duration of aortic occlusion (h)	5.5 (1.8–17.3)	0.003
Surgeon's assessment of revascularization: poor or fair (not good or excellent)	2.3 (0.7–8.1)	0.200
Intraoperative ST segment depression	3.9 (1.2–12.6)	0.021
Intraoperative ST segment elevation	7.1 (2.7–19.0)	0.0001
Intraoperative ST segment depression or elevation	6.8 (2.8–16.9)	0.0001
Minutes of post-CPB HR > 110 beats/min (per 10 min)	1.3 (0.9–1.9)	0.186

CPB = cardiopulmonary bypass; HR = heart rate.

Discussion

During perioperative Holter monitoring, 58% patients had ST segment deviation, major cardiac conduction change (≥30 min), or use of ventricular pacing (≥30 min), all of which were most prevalent in the first 8 h after release of aortic occlusion. Episodes of ST segment deviation occurred in 33% patients. These findings are similar to those previously described by us[9,14] in patients having CABG surgery who received propofol-sufentanil or sufentanil-midazolam anesthetics. Because serum CK-MB generally peaked by 16 h after the release of aortic occlusion, most MI occurred in this period. Electrocardiographic abnormalities were the strongest predictors of MI and may have been caused by myocardial necrosis. This points to the need for detailed ECG monitoring. Reduction of ECG changes can be one of the criteria used to optimize clinical care.

Changes on the Holter Electrocardiogram

Because many changes were observed on the ECG, we carefully applied the criteria to identify the major changes reported. Small QRS complex, conduction changes, and ventricular pacing were most prevalent soon after the end of cardioplegic arrest and subsided gradually in the next few hours. This finding suggests

Table 7. Multivariable Models of Association with (Q Wave and CK-MB) or Autopsy Myocardial Infarction (n = 566)

Predictor	Odds Ratio (95% Confidence Interval)	Coefficient	Standard Error	*P* Value
Intraoperative ST segment elevation	8.1 (2.9–23.0)	2.10	0.53	0.0001
Intraoperative ST segment depression	4.2 (1.2–14.1)	1.42	0.62	0.022
Duration of aortic occlusion (h)	5.7 (1.8–17.9)	1.73	0.59	0.003
Constant		−5.35	0.76	

that these changes occurred primarily during cardioplegic arrest, reperfusion, or soon after these events. In contrast, although some episodes of ST segment deviation were observed with restoration of cardiac rhythm after cardioplegic arrest, most began minutes to hours later. Thus post-CPB causes contributed to the occurrence of most episodes of ST segment deviation.[15]

Substantially more episodes of ST segment deviation would have been detected in the first 8 h after release of aortic occlusion if they were not masked by ST segment deviation due to cardiac conduction change and ventricular pacing, which were also most prevalent in the same period (fig. 1). The reduced QRS amplitude in this period also decreased the likelihood of ischemia causing a ST segment deviation of at least 1 mm. Detection of changes on the ECG was limited by the leads monitored and by changes in the chest wall. The right ventricle and the anteroseptal wall of the left ventricle were inadequately monitored.[2,16]

Heart rate at the onset of episodes of ST segment depression was greater in the postoperative period than in the preoperative period (fig. 2E). This resetting of the threshold for HR is similar to that reported in ambulatory patients.[17] In the post-CPB and postoperative periods, a few of the episodes of ST segment deviation occurred when HR was fixed by atrial pacing.

Myocardial Infarction

Significance of Myocardial Infarction. The functional and prognostic significance of myocardial necrosis depends on various factors, including size, location, condition of the myocardium, and whether necrosis is diffuse or localized. This hinders the development of widely applicable criteria for MI. Different criteria may be suitable in different settings. During CABG surgery, diffuse myocyte necrosis and necrosis in the distribution of multiple small-caliber coronary arteries may occur.[18,19] Such necrosis may not lead to ST segment deviation or a new Q wave, but it increases serum CK-MB and may adversely affect function and prognosis. The use of (Q wave and CK-MB) or autopsy criteria for MI may detect only large MI and miss large areas of myocardial necrosis in many patients.

Myocardial infarction detected by the criteria we used have been shown previously to adversely affect function and prognosis. A new significant Q wave[20–22] or increased CK-MB[20] are reported to be associated with reduced survival. Q wave MI detected by Minnesota coding is likely to be confirmed by autopsy.[23] CK-MB > 133 U/l is reported to be associated with autopsy criteria for MI[24] and to correspond approximately to the threshold of CK-MB > 100 ng/ml[25] used in our study. Patients with anterior or anterolateral Q wave MI had reduced postoperative EF in our study (table 2).

Perfusion to the MI occurring during revascularization is increased, unlike perfusion to other MI. Thus the MIs we detected are likely to cause fewer adverse effects than MIs in patients not having revascularization. However, in the setting of percutaneous transluminal coronary angioplasty, even minor elevation of the serum CK-MB level has been shown to be associated with increased incidence of cardiac death and other cardiac complications on follow-up over 3 yr.[26,27]

Incidence of Myocardial Infarction. The incidence of MI depends critically on the methods of and criteria for detection.[1–8,18–25,28,29] Although patients with increased CK-MB are reported to have adverse prognosis,[20,24] many studies have not used enzymatic criteria to detect MI.[21,22,28,29] Our incidence of meeting Q wave criteria for MI is within the range reported previously.[21,22,28,29] Despite the use of conservative thresholds for CK-MB, our incidence of meeting CK-MB criteria for MI (21%) is greater than that reported in the past.[4,20] A recent multicenter trial[30] of 2,682 patients (Acadesine Trial #1024) found the incidence of (Q wave and CK-MB) or autopsy MI to be similar to that in our present study. In these 2,682 patients, the CK-MB increase was similar to that in our present study.

Our results indicate that when uniform methods of and criteria for detecting MI are used, there is substantial variability in the incidence of MI at different clinical sites. Institutions with a low incidence of MI may be more inclined to publish it in their single-center studies. Previous multicenter studies reporting the incidence of MI generally have allowed each clinical site to have its own method of and criteria for detecting MI.[20]

In our study, a single CK-MB sample drawn between 8 and 24 h after the release of aortic occlusion led to a 10.8–9.3% incidence of CK-MB ≥ 100 ng/ml, suggesting that inadequate sampling of CK-MB may lead to identification of only approximately half of the patients who meet our CK-MB criteria for MI. Our results show that to determine the incidence of an outcome such as MI, a protocol for detailed data collection at multiple representative clinical sites and analysis at core laboratories must be used. A high incidence of MI during CABG surgery would explain why, compared with medical therapy, CABG surgery does not provide a long-term survival advantage to patients who are not in high-risk categories of coronary artery disease (CAD).[31] The high incidence of myocardial ischemia and MI observed after CPB points to the need to modify the conduct of CPB and to use safer techniques when possible.

False-positive diagnosis of MI may occur because increased CK-MB may be due to incisions in the atria and skeletal muscles. However, peak CK-MB after uncomplicated cardiac and major noncardiac surgery is reported generally to be substantially less than 100 ng/ml.[2] Significant Q waves after CABG surgery may be caused by unmasking of an old MI[32] or may be unrelated to MI. The 19% patients who met Q wave or CK-MB or autopsy criteria for MI and had both increased CK-MB and major ECG changes are very likely to have had substantial myocardial necrosis.

Electrocardiographic Lead Groups. Q wave MI after CABG surgery has been reported[29] to be most common in the inferior leads, as we also observed. The significance of inferior Q wave has been questioned because of a limited association with wall-motion abnormality detected with echocardiography.[29] In our study, 80% of the patients who developed Q wave in the anterior or anterolateral lead groups and 67% of the patients who developed Q wave in the inferior lead group had peak CK-MB levels greater than 59 ng/ml (mean + SD of the peak CK-MB value in patients in the No Abnormality group in table 2). The values of peak CK-MB were comparable in patients with ST segment deviation in the anterior or anterolateral leads (CM_5, CC_5) and inferior (ML) lead. It was uncommon for episodes of ST segment depression to be assigned to lead ML and ST segment elevation to lead CC_5.

Timing of Occurrence of Myocardial Infarction. Among the 44 patients who met Q wave criteria for MI, a new Q wave was first recorded immediately after surgery in 39% and by the morning of POD 1 in 80% of patients. Peak serum CK-MB concentration occurred within 16 h of release of aortic occlusion in approximately 70% of the patients who had MI (table 2). Clinical care in this period should be optimized to minimize the incidence of MI.

Predictors of Myocardial Infarction

Intraoperative ECG changes and duration of post-CPB hypotension were independent predictors of Q wave or CK-MB or autopsy MI, whereas most of the demographic and clinical variables were not selected (table 5). This establishes the incremental value of ECG and hemodynamic monitoring to predict Q wave or CK-MB or autopsy MI. It also suggests that the risk of MI depends primarily on the perioperative course rather than on the patient's preoperative status. This is also suggested by the association of Q wave or CK-MB or autopsy MI with duration of CPB and the surgeon's assessment of revascularization (table 4), which is similar to some previous reports.[4] However, the previous studies[8] of predictors of MI generally have not evaluated the intraoperative predictors in detail. Fewer significant predictors of (Q wave and CK-MB) or autopsy MI were identified, in part, because of the smaller number of patients with such MI.

Holter Electrocardiographic Changes. The association with MI of intraoperative ST segment deviation (tables 4–7) and the elevated peak CK-MB in patients with ST segment deviation (table 2) suggest that many episodes of ST segment deviation may be due to myocardial necrosis, similar to that in ambulatory patients with acute MI.[16,33] Compared with ST segment depression, ST segment elevation was associated with more severe necrosis. The magnitude of ST segment deviation in excess of 1 mm did not correlate with the severity of necrosis (table 2), possibly because of the reduced QRS amplitude after CPB. The episodes of ST segment deviation were identified after eliminating ST segment deviation due to nonischemic causes. Episodes of ST segment deviation starting or ending during operation were used in tables 4–7 because in a clinical setting more careful

ECG monitoring is often performed during operatively than before or afterward.

ST segment deviation may be used to estimate the timing of some myocardial injuries and thus their proximate triggers. In contrast to previous studies,[4] in our patients preoperative ST segment deviation (table 3) or preoperative history of unstable angina (tables 4 and 6) were not associated with MI. Two patients having repeated operation may have had MI at the time of ST segment elevation in the pre-CPB period.[2,34] Table 3 and CK-MB release pattern suggest that few other MIs occurred in the pre-CPB period. The strong association with MI (table 3) of episodes of ST segment deviation occurring minutes to hours after the release of aortic occlusion suggests that most of the MIs were triggered in this period in patients rendered susceptible by CPB.[1,2,15] For patients who met Q wave criteria for MI, HR at the onset of episodes of ST segment deviation occurring after release of aortic occlusion was less than the baseline HR. This indicates that a reduction in myocardial oxygen supply was an important mechanism of development of Q wave.[1,2,15] Intraventricular conduction defect and LBBB may also be indicative of the occurrence of myocardial necrosis (tables 2, 4, 5), as in ambulatory patients. Such necrosis may occur during CPB, reperfusion, or soon after those events.

Prolonged ECG changes were associated with a greater incidence of MI (fig. 3), consistent with previous reports.[35,36] This suggests that a therapeutic intervention that corrects the abnormality causing a new ECG change may reduce the incidence of MI. This confirms the utility of ECG monitoring.

Hemodynamic Abnormalities. Morbidity including MI is more likely in patients with lower blood pressure during CPB.[37] Post-CPB hypotension and tachycardia are reported to be associated with left ventricular wall-motion abnormality, which is associated with MI.[3,38] In our study, the values of blood pressure were affected by site-specific equipment and patient-specific hydraulics of the monitoring systems. In addition, only baseline blood pressure was not obtained invasively. These factors are unlikely to alter the conclusion that post-CPB hypotension is associated with Q wave or CK-MB or autopsy MI because the association was demonstrated for a wide range of thresholds. Hemodynamic abnormalities occurred despite usual attempts to maintain stability. Only a controlled clinical trial testing more than one range of hemodynamics can determine if more intensive efforts to maintain hemodynamics within a certain range would reduce the incidence of MI. Hemodynamic abnormalities were not shown to be associated with (Q wave and CK-MB) or autopsy MI, possibly because of the small number of patients with such MI.

Previously, we found a high incidence of intraoperative episodes of hemodynamic abnormalities lasting at least 5 min and a lack of temporal association of these episodes with new ST segment deviation.[9] Hence, overall burden of hypotension and tachycardia after CPB, rather than isolated episodes, may be the determinant of fulfilling CK-MB criteria of MI. Because hypotension and tachycardia occurring only in the post-CPB period were shown to be associated with Q wave or CK-MB or autopsy MI, maintenance of adequate hemodynamics is important, especially when increased susceptibility to MI exists.

Comparison with Other Populations

ST segment elevation, although common in patients with acute MI[33] and occurring in 13% of our patients, is rare in patients with CAD or risk factors for CAD who are undergoing major noncardiac surgery[39,40] and in ambulatory patients with stable[41] or unstable angina.[35] New cardiac conduction change, ventricular pacing, and small QRS complex are common in our population, but not in the other previously mentioned populations. In patients with CAD or risk factors for CAD who are undergoing major noncardiac surgery, intraoperative ischemia is less severe than in our patients[39]; the greatest incidence of ST segment deviation is observed on awakening from general anesthesia, and there is a substantial incidence of ST segment deviation for at least 1 week after surgery.[6,39,40,42]

The incidence of MI in our patients is substantially greater than that in patients with CAD or risk factors for CAD who are having major noncardiac surgery.[6,42] Unlike our patients, patients undergoing noncardiac surgery usually do not have unstable angina. However, as can be deduced from tables 4 and 6, the incidence of MI in the 40% of our patients who had a history of unstable angina was not significantly greater than that in the remaining patients. After noncardiac surgery, most MIs occur 2 or more days after surgery.[6,42] The difference in the timing of MI after cardiac and noncardiac surgeries suggests that the primary mechanisms of MI for the two populations are different.

The association of ST segment deviation with MI in our population was comparable to that in ambulatory patients with suspected acute MI,[33] stronger than that reported for patients with CAD or risk factors for CAD undergoing major noncardiac surgery,[6,42] and for ambulatory patients with stable[41] or unstable[35] angina.

Limitations of the Study

Combining patients who received acadesine or placebo may have influenced specific results but did not alter our primary conclusions. The predictors of MI and various other results are likely to be different at different clinical sites, although the results obtained from pooled data are presented. The lack of hemodynamic and EF data for a subset of patients was due to logistical concerns and is unlikely to have introduced a systematic bias in our results. Ejection fraction data are limited by the use of different methods of measurement for the preoperative and postoperative values and by lack of analysis at a core laboratory. Limitations of the Holter ECG and hemodynamic monitoring systems have been discussed previously. The serum CK-MB value as a measure of the extent of myocardial necrosis is limited by CK-MB release from incisions in the skeletal muscles and atria and by the variability of reperfusion of the necrotic myocardium. A lack of data for postoperative SBP, DBP, and HR and perioperative left ventricular filling pressure prevented evaluation of their potential predictive value for MI. The need to maintain SBP and HR within certain ranges was not established in this study. A lack of long-term follow-up limited our ability to determine the functional and prognostic significance of MI. This study did not evaluate the suitability of different criteria for MI.

Conclusions

Detailed multicenter data collection and analysis at core laboratories detected substantial site-to-site variability in the incidence of MI and an overall incidence of up to 25%. Most MIs were triggered by events occurring minutes to hours after the release of aortic occlusion and were strongly associated with major ECG changes also occurring primarily during this period. During perioperative monitoring, 58% of the patients had major ECG changes.

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Appendix I. Clinical Sites and Principal Investigators

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University of California, San Francisco	Jacqueline Leung, M.D.
Cedars-Sinai Medical Center	Arnold Friedman, M.D.
Cleveland Clinic	Norman Starr, M.D.
Cornell University	Onofrio Patafio, M.D.
Creighton University	Syed Mohiudden, M.D.
Deborah Heart Institute	Mark Adkins, M.D.
Duke University	Thomas Stanley, M.D.
Kaiser Permanente Medical Center, San Francisco	Wayne Bellows, M.D.; Gary Roach, M.D.; John Reeves, M.D.
Massachusetts General Hospital (Harvard)	Michael D'Ambra, M.D.
University of Michigan	Joyce Wahr, M.D.
New York University	Katherine Marschall, M.D.
Stanford University	Lawrence Siegel, M.D.
Medical College of Virginia	Judith Fabian, M.D.
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Western Pennsylvania Hospital	Alan Gradman, M.D.
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Appendix II. Core Laboratories

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CK-MB analysis was performed by SmithKlineBeecham, Inc., Van Nuys, CA. Many persons at the clinical sites, core laboratories, and Gensia, Inc. contributed to collection of the data.