Anesthesiology
70:230–236, 1989

The Incidence of Myocardial Ischemia during Anesthesia for Coronary Artery Bypass Surgery in Patients Receiving Pancuronium or Vecuronium

J. P. O'Connor, M.D., J. G. Ramsay, M.D.,* J. E. Wynands, M.D.,† F. E. Ralley, M.D.,* W. F. Casey, M.D.,‡ C. E. Smith, M.D.,* G. R. Robbins, M.D.,* J. Bilodeau, B.Sc.N.,§ M. H. Sami, M.D.¶*

This study was performed to compare the incidence of prebypass myocardial ischemia in patients receiving fentanyl and enflurane for anesthesia along with either pancuronium or vecuronium. Ninety-eight patients with normal left ventricular function were randomly allocated to receive either pancuronium 0.15 mg·kg^{-1} or vecuronium 0.15 mg·kg^{-1} in a double-blind manner after fentanyl 40 μg·kg^{-1} for induction of anesthesia for elective coronary artery bypass grafting (CABG). Premedication included diazepam 0.15 mg·kg^{-1} po, morphine 0.10 mg·kg^{-1}, and scopolamine 0.005 mg·kg^{-1} im. Two lead Holter monitor recordings (leads V_6 and V_9) from the time of arrival in the operating suite to institution of cardiopulmonary bypass were analyzed for ischemia by a cardiologist blinded to the choice of muscle relaxant. Intraoperatively, heart rates greater than 90 beats·min^{-1} and systolic blood pressure ± 20% of ward values were treated with propranolol, enflurane, or phenylephrine. Nitroglycerin was infused for ECG signs of ischemia or pulmonary hypertension. After induction of anesthesia the heart rate and cardiac index were consistently decreased in patients receiving vecuronium and also lower in these patients compared with those receiving pancuronium. Thirty-two per cent of patients receiving pancuronium received propranolol for heart rates >90 beats·min^{-1} versus 7% of those who received vecuronium ($P \sim 0.01$). Eight patients developed 13 episodes of ischemia after administration of the muscle relaxant: four who received pancuronium (n = 44; 9%) and four receiving vecuronium (n = 54; 7%). Four episodes occurred at induction or tracheal intubation, two in each group. There were four perioperative myocardial infarctions as determined by ECG and CPK-MB levels, two in each group. None of these four patients had prebypass ischemia. Either pancuronium or vecuronium may be used with fentanyl for CABG with a low incidence of ischemia, although patients receiving pancuronium require treatment for tachycardia more frequently. (Key words: Anesthetics, intravenous: fentanyl. Neuromuscular relaxants: pancuronium; vecuronium. Monitoring: myocardial ischemia; Holter. Surgery: Cardiac.)

PANCURONIUM is widely employed in cardiac anesthesia to produce skeletal muscle paralysis.[1,2] Recently, Thomson and Putnins showed that the use of pancuronium in patients having coronary artery bypass graft (CABG) surgery may cause significant elevations in heart rate and ECG evidence of ischemia.[2]

Studies from this institution have reported an incidence of ischemia of 13% and 26% using either fentanyl or sufentanil as the opiate and pancuronium as the muscle relaxant.[3,*] Because a relationship between prebypass ischemia and perioperative myocardial infarction (MI) may exist,[1] a reduction in the incidence of prebypass ischemia should reduce the incidence of myocardial infarction.

Vecuronium is a muscle relaxant with fewer cardiovascular side effects than pancuronium.[4–6] In contrast to pancuronium, tachycardia has not been reported to occur with vecuronium at four times the usual clinical dose.[6,7] Because prebypass ischemia has been reported to occur more frequently in association with tachycardia,[1] it follows that vecuronium may be superior to pancuronium for muscle relaxation during anesthesia for CABG surgery.

This study was designed to compare the incidence of prebypass ischemia associated with the use of pancuronium versus vecuronium in patients receiving a moderate dose narcotic technique of anesthesia for CABG surgery.

Methods

With Ethics Committee approval, 100 patients scheduled for elective CABG surgery were studied. Informed patient consent was not required by the committee because the protocol did not deviate from normal clinical practice. All patients had left ventricular ejection fractions (LVEF) greater than 0.4. All cardiac medications were continued until surgery, and premedication consisted of oral diazepam 0.15 mg·kg^{-1} 1.5 h before surgery and morphine 0.1 mg·kg^{-1} with scopolamine 0.005 mg·kg^{-1} intramuscularly 1 h before surgery. Thirty minutes before surgery a continuous ECG recording monitor (Holter) was applied to each patient using a dual electrocardiographic battery operated Reynolds Tracker 2™ cassette recorder (Reynolds Medical Ltd., Hertford, England).

* Assistant Professor, Anaesthesia.
† Professor, Anaesthesia and Surgery.
‡ Clinical Fellow in Anaesthesia.
§ Research Assistant, Anaesthesia.
¶ Associate Professor, Medicine (Cardiology).

Received from the Departments of Anaesthesia and Cardiology, Royal Victoria Hospital and McGill University, Montreal, Quebec, Canada. Accepted for publication September 12, 1988. Presented at 1987 Annual Meetings of the Society of Cardiovascular Anesthesiologists, Palm Desert, California and the Canadian Anesthetists' Society, Calgary, Alberta, Canada.

Address reprint requests to Dr. O'Connor: Department of Anaesthesia, Royal Victoria Hospital, 687 avenue des Pins Quest, Montreal, Quebec, Canada H3A 1A1.

* Litak CA, Ralley FE, Wynands JE, Ansley DM, Sami MH: Hemodynamic variables and the incidence of prebypass ischemia during sufentanil/O/pancuronium anesthesia in patients undergoing coronary artery surgery. J Cardiothorac Anesth 1:10–18, 1987.

Positive electrodes were placed on the 6th rib at the mid axillary line for channel 1 and on the same transverse plane 1.5 cm to the left of the spinal column for channel 2. The two negative electrodes were attached to the right shoulder. This allowed continuous recordings of modified leads V_6 and V_9. This configuration allowed detection of left ventricular ischemia without encroaching on the surgical field[3] while the V_5 lead was monitored by the attending anesthesiologist. The patients were then rested for 15 min so that a control ECG (Holter leads V_6 and V_9) could be obtained. The Holter recording was synchronized to operative procedures with a recorder clock channel to mark events in the prebypass period.

Upon arrival in the operating room, modified V_5 (CS5) and standard lead II ECG monitor electrodes were attached. Peripheral venous, radial arterial, and internal jugular vein catheters were inserted under local anesthesia. Increments of 2.5 mg iv of diazepam were given if needed for additional sedation during these procedures. A thermodilution pulmonary artery catheter was inserted *via* the internal jugular vein cannula, and preoperative measurements of the central venous, pulmonary artery, and pulmonary capillary wedge pressures and the cardiac output were made. Ward values of heart rate and blood pressure were acquired retrospectively from the hospital chart by an observer blinded to the relaxant given, and represent an average of the measurements made by the nursing staff prior to premedication.

Induction of anesthesia was with fentanyl 40 $\mu g \cdot kg^{-1}$ given over 3 min. Muscle relaxants were administered in a randomized, blinded fashion such that each patient received a total dose of 0.15 $mg \cdot kg^{-1}$ of either pancuronium or vecuronium (approximately three times the effective dose to produce 95% twitch depression[8]). The muscle relaxants were given in divided doses, the first dose (0.03 $mg \cdot kg^{-1}$) 60 s before the fentanyl; the second dose (0.12 $mg \cdot kg^{-1}$) was given over 10 s following loss of response to verbal command. Ventilation was assisted then controlled. End-tidal CO_2 concentration was measured using a Hewlett Packard CO_2 analyzer (model #4360A, Hewlett Packard, Walthern, Massachusetts) or a SARA™ mass spectrometer (Allegany International Medical Technology, St. Louis, Missouri) and kept between 30 and 40 mmHg. Tracheal intubation was performed 3 min after the fentanyl infusion was completed. Further hemodynamic measurements were made 1 min postinduction, 1 and 10 min postintubation, at sternotomy, and at aortic dissection by a nonparticipating observer. Systolic blood pressure increases or decreases of greater than 20% from ward values were treated with enflurane or incremental doses of phenylephrine (50 μg), respectively. Heart rates of greater than 90 beats $\cdot$ min^{-1} were treated with incremental doses of propranolol (0.5 mg). Nitroglycerin was infused if changes suggestive of myocardial ischemia were seen on the ECG monitor, or to treat episodes of pulmonary hypertension. Surgery was performed by one of four surgeons, all of whom utilized cold potassium cardioplegia and topical cooling for myocardial preservation.

TABLE 1. Patient Demographics

	Pancuronium (n = 44)	Vecuronium (n = 54)
Age (yr)	58.3 ± 1.6	60.0 ± 1.3
Sex M/F	38/6	43/11
Height (cm)	171.6 ± 1.2	168.5 ± 1.2
Weight (kg)	82.1 ± 2.0	75.7 ± 1.6*
BSA (M^2)	2.0 ± 0.03	1.9 ± 0.02*
LVEF (%)	52.4 ± 1.3	57.1 ± 1.8
Diseased vessels (range)	2.61 (1–4)	2.93 (1–5)
Grafted vessels (range)	3.3 (1–5)	3.5 (1–5)
Prebypass time (min)	129.0 ± 4.4	123.4 ± 3.9
Aortic crossclamp (min)	56.8 ± 3.8	61.1 ± 2.9
Total bypass (min)	89.2 ± 4.4	83.6 ± 4.1
Preoperative blocking drugs		
Beta adrenergic n(%)	30 (68)	38 (69)
Calcium channel n(%)	36 (82)	45 (78)
Intraoperative medication		
Propranolol		
n(%)	14 (32)	3 (6)*
(mg)	2.82 ± 0.46	1.67 ± 0.67
Diazepam		
n(%)	5 (11)	9 (17)
(mg)	3.5 ± 1	2.44 ± 0.05
Phenylephrine		
n(%)	9 (21)	7 (13)
μg	100 ± 22.05	92.9 ± 7.14
Nitroglycerine		
n(%)	15 (34)	19 (35)
Enflurane		
n(%)	32 (73)	36 (67)

Values are mean ± SEM (if not stated otherwise).
* $P < 0.05$ *vs.* pancuronium.

Analysis of the Holter recordings was with a Reynolds Pathfinder™ analyser and trend system fitted with Replay 2 and Playback™.[10] A cardiologist blinded to the muscle relaxant given analyzed the recordings. Ischemia was defined as a new 1-mm ST segment depression from baseline, measured 80 ms from the J point, lasting at least 30 s.

The diagnosis of perioperative MI was made by the same cardiologist again in a blinded fashion, using myocardial creatine phosphokinase (CPK-MB) fractions collected in the first 24 h, and the serial postoperative electrocardiograms. An MI was diagnosed when any CPK-MB was greater than 60 IU in association with either new Q waves or progressive ST and T wave changes suggestive of evolving MI.

The data were analyzed using analysis of variance. Unpaired *t* test with Bonferroni correction was used for intergroup comparisons, and paired *t* test with Bonferroni

TABLE 2. Hemodynamic Data (mean ± SEM)

	Ward	Baseline	Induction	Postintubation 1 min	Postintubation 10 min	Incision	Sternotomy	Aortic Dissection
HR (beats · min^{-1})								
P	69 ± 1.42*	61 ± 1.63	64 ± 2.22	73 ± 2.03*	67 ± 1.64*	62 ± 1.46	61 ± 1.66	65 ± 1.59
V	67 ± 1.38*	60 ± 1.35	55 ± 1.27*†	59 ± 1.54*†	52 ± 1.21*†	50 ± 1.36*†	48 ± 1.22*†	56 ± 1.44*†
MAP (mmHg)								
P	94 ± 1.68*	87 ± 2.16	80 ± 2.59*	85 ± 2.20	80 ± 2.07*	80 ± 1.70*	85 ± 2.03	84 ± 2.01*
V	97 ± 1.54	92 ± 2.15	83 ± 2.33*	84 ± 2.03*	81 ± 1.91*	82 ± 1.67*	87 ± 1.82	87 ± 1.98*
SBP (mmHg)								
P	129 ± 2.57*	141 ± 3.48	126 ± 3.72*	134 ± 3.71	127 ± 2.57*	124 ± 1.96	131 ± 2.53*	126 ± 2.45
V	134 ± 2.68*	150 ± 3.51	132 ± 3.64*	137 ± 3.22*	130 ± 2.95*	129 ± 2.58	135 ± 2.68*	131 ± 2.85
MPAP (mmHg)								
P		19 ± 0.96	18 ± 0.67	19 ± 0.74	16 ± 0.60	16 ± 0.64	16 ± 0.58	16 ± 0.66
V		20 ± 0.84	19 ± 0.70	19 ± 0.60	17 ± 0.57	16 ± 0.60	16 ± 0.59	15 ± 0.68
PCWP (mmHg)								
P		12 ± 0.73	11 ± 0.64	10 ± 0.62	9 ± 0.50*	10 ± 0.54	10 ± 0.42	10 ± 0.61
V		12 ± 0.75	12 ± 0.56	11 ± 0.58	10 ± 0.51	11 ± 0.50	10 ± 0.59	9 ± 0.59
CVP (mmHg)								
P		6 ± 0.57	6 ± 0.43	6 ± 0.41	6 ± 0.41	6 ± 0.42	6 ± 0.39	6 ± 0.44
V		6 ± 0.57	7 ± 0.54	7 ± 0.52	7 ± 0.48	7 ± 0.52	7 ± 0.50	6 ± 0.50
C.I. (l · min^{-1} · m^2)								
P		2.71 ± 0.09	2.89 ± 0.12	2.93 ± 0.11	2.63 ± 0.09	2.56 ± 0.08	2.61 ± 0.08	2.38 ± 0.08*
V		2.70 ± 0.08	2.50 ± 0.08†	2.40 ± 0.07*†	2.16 ± 0.06*†	2.22 ± 0.06*†	2.24 ± 0.07*†	2.13 ± 0.07*

P = pancuronium (n = 44); V = vecuronium (n = 54).
* $P < 0.05$ from baseline.
† $P < 0.05$ between groups.

correction was used for intragroup comparisons. Chi-square analysis with Yates correction was used for proportions. A P value of less than 0.05 was considered significant.

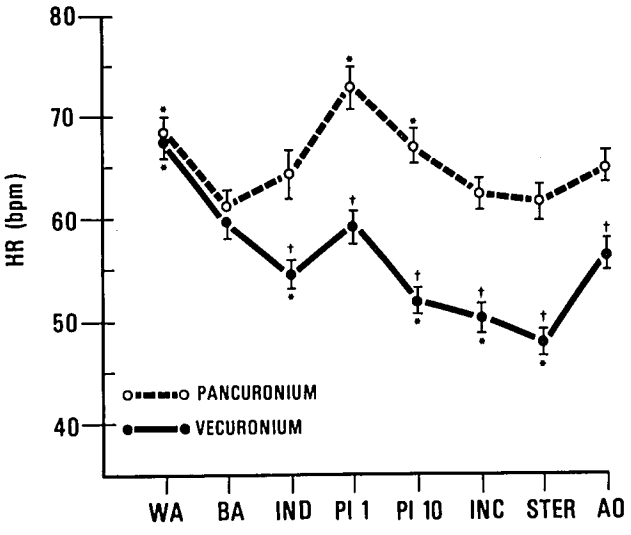

FIG. 1. Heart rate (mean ± SEM) at measurement intervals of the study. WA = ward; BA = baseline operating room; IND = induction; PI 1 = 1 min post intubation; INC = skin incision; PI 10 = 10 min post intubation; STER = sternotomy; AO = aortic dissection. *Significantly different from baseline, $P < 0.05$. †Significantly different from pancuronium, $P < 0.05$.

Results

The final study comprised 98 of the 100 patients entered into the study. One patient (no prebypass ischemia) was deleted because complete measurements from baseline were not available. A second patient was deleted because an intraventricular conduction delay, which developed between the preop ECG and the placement of the Holter monitor, prevented accurate interpretation of the ST segments. Forty-four patients received pancuronium and 54 patients received vecuronium (a result of the random number assignment). Demographic data for each patient group are presented in table 1. Despite randomization the vecuronium group had a greater weight and body surface area.

Hemodynamic data are presented in table 2, and figures 1 and 2. The mean heart rate at baseline (arrival in OR) was lower than that obtained on the ward in both groups. In patients in the vecuronium group the heart rate continued to decrease, being lower than baseline at all times. In the pancuronium group the heart rate was significantly higher than baseline 1 and 10 min postintubation, and higher than in patients in the vecuronium group at all times after baseline (fig. 1). The cardiac index was decreased from baseline at all times postinduction in the vecuronium group, and lower than that in the pancuronium group after intubation until sternotomy (fig. 2).

Ten patients developed 16 episodes of ischemia (table

3). In every instance ischemia was found on the V_6 lead; in one patient both V_6 and V_9 reflected ischemia. Two patients receiving pancuronium developed ischemia only during insertion of monitoring catheters. Four patients receiving pancuronium (9%) and four patients receiving vecuronium (7.4%) developed ischemia postinduction (NS). Fifteen patients receiving pancuronium (34%) and 19 patients receiving vecuronium (35%) received intraoperative therapy with iv nitroglycerin prebypass (NS). Fourteen patients receiving pancuronium (32%) versus four patients receiving vecuronium (7%) required intraoperative beta adrenergic blocking drug therapy to control heart rates greater than 90 beats · min^{-1} ($P < 0.01$). Two postoperative MIs occurred in each group (pancuronium 4.5%, vecuronium 3.6%), and none of these patients had prebypass ischemia. The only difference between those patients with a postoperative MI and the rest of the study population was a significantly longer aortic cross clamp time (73 ± 3.5 min *vs.* 58 ± 2 min; $P < 0.05$) in the four patients with an infarction.

One patient who received pancuronium died 24 h postoperatively of an asystolic cardiac arrest. This patient did not show prebypass ischemia, nor was a perioperative myocardial infarction diagnosed by our criteria. An autopsy was denied by the family.

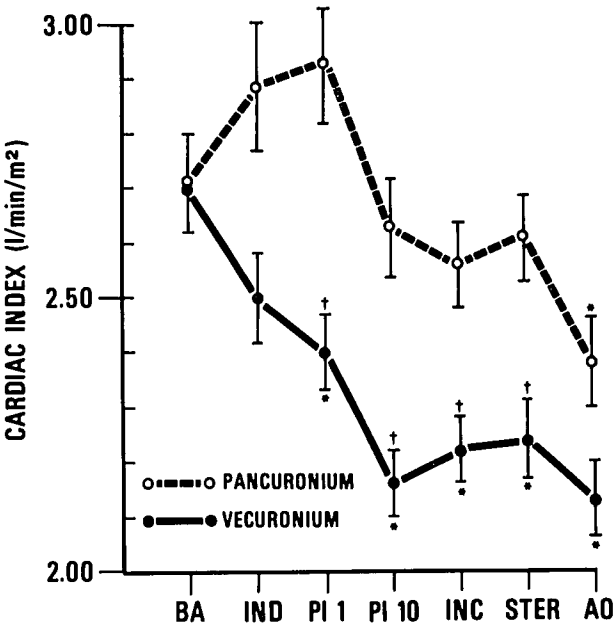

FIG. 2. Cardiac Index (mean ± SEM) at measurement intervals. Intervals are as per figure 1. *Significantly different from baseline, $P < 0.05$. †Significantly different from pancuronium, $P < 0.05$.

Discussion

This study demonstrates that when either pancuronium or vecuronium was used as the muscle relaxant for CABG surgery, and when a heart rate >90 beats · min^{-1} is promptly treated with propranolol there was a similar low incidence of prebypass ischemia (pancuronium 9%, vecuronium 7%). There was no correlation between prebypass ischemia and perioperative MI; however, the four

TABLE 3. Ischemic Episodes

MR	Ward, BP, HR	Duration	Event	Associated BP and HR	Rx
Pancuronium	110/63, 92	8 min	Monitoring catheter insertion	141/78, 90	—
Pancuronium	127/80, 82	15 min	Aortic dissection	170/90, 85	Enflurane
Pancuronium	130/80, 72	8 min 5 min	Postinduction and intubation sternotomy	133/60, 94 160/74, 73	Propranolol
Pancuronium	140/78, 70	6 min*	Monitoring catheter insertion	165/65, 79	SL + IV NTG
Pancuronium	110/72, 55	12 min* 5 min	Sternotomy Aortic dissection	124/60, 58 139/68, 70	— —
Pancuronium	150/80, 68	3 min* 5 min* 5 min*	Postintubation Incision Internal mammary artery dissection	132/53, 55 150/57, 51 135/56, 55	— NTG for 2nd and 3rd episodes
Vecuronium	170/80, 59	18 min 37 min	Postinduction and intubation Sternotomy	100/40, 54 114/65, 64	NTG infusion —
Vecuronium	125/80, 60	17 min	Sternotomy	170/68, 70	—
Vecuronium	170/80, 78	10 min*	Intubation	140/57, 51	NTG Infusion
Vecuronium	140/70, 80	23 min 3 min	Arrival and monitoring catheter insertion Aortic dissection	115/53, 96 110/58, 70	SL NTG —

* Episode of ischemia unrelated to hemodynamic changes.

patients (4%) who did develop infarction had a significantly longer aortic crossclamp time.

In both groups a significant decrease in heart rate was seen following premedication (fig. 1). In the pancuronium group the heart rate increased significantly at intubation and remained elevated 10 min after intubation. This is consistent with previous reports.[2,7,10] Thirty-two per cent of these patients received propranolol to reduce their heart rate to less than 90 beats/min. The consistently reduced heart rate in the patients receiving vecuronium may represent increased vagal tone, unopposed by agents like pancuronium. A high dose of fentanyl causes a decrease in heart rate, which can be prevented by vagotomy in dogs.[11] Alternatively, the reduction in heart rate may be a direct effect of vecuronium.[12]

The 9% incidence of prebypass ischemia in patients receiving pancuronium differs from the 25%[2] and 50%[13] incidence previously reported with fentanyl anesthesia when pancuronium was used as the muscle relaxant. The incidence of ischemia in this study is also lower than the 36% and 41% reported by Slogoff where pancuronium was combined with various anesthetic agents for CABG surgery.[1,14] Two of the three patients who developed ischemia and who received pancuronium in Thomson's study developed increases in heart rate of more than 50%.[2] Similarly, in the 1985 study by Slogoff and Keats,[1] ischemia occurred significantly more frequently in patients who developed tachycardia as defined by a heart rate of greater than 100 beats $\cdot$ min^{-1}. In their more recent study ischemia was again significantly associated with a heart rate >110 beats $\cdot$ min^{-1}.[14] No standard approach was taken in response to hemodynamic changes in any of these studies. We treated a heart rate increase of greater than 90 beats $\cdot$ min^{-1} with iv propranolol, and also promptly treated changes in blood pressure of ±20%. We feel this prompt treatment of tachycardia and blood pressure changes is the major reason for the lower incidence of ischemia as compared with that in other reports.

An alternative explanation for the low incidence of ischemia in this study might be that leads V_6 and V_9 are not as sensitive as other reported lead combinations used to detect intraoperative ischemia. Until the recent report by London *et al.*[15] (published after the present work was completed), there was little evidence to support the superiority of any recording system. Based on an exercise study by Blackburn and Katigbak,[16] Thys and Kaplan[17] have recommended that leads V_5 (or a bipolar equivalent) and II be monitored. Slogoff and Keats utilized these latter leads, while Thomson recorded leads CS5 and II; other investigators have used CM5 and II,[18] or CC5 with either CM5 or modified ML lead[19] (conforming to Mason-Likar standard lead II[20]).

Blackburn and Katigbak[16] found 89% of the ischemia detected in a 6 lead system after exercise to be present in V_5, versus 70% in V_6. In a more extensively documented report, however, Mason *et al.*[21] found a similar incidence of ischemia during exercise or postexercise in both V_5 and V_6, and "in those subjects in whom only a single lead was positive . . . lead V6 again was most often of value." In another exercise study, Sketch *et al.*[22] found similar sensitivities in leads V_5 and V_6 (61% and 60%, respectively). In contrast, the recent study by London *et al.*,[15] using continuous 12 lead computerized ECG recording in patients undergoing noncardiac surgery but with known or suspected coronary disease, found only a 37% sensitivity of V_6 compared with 75% for V_5 in 25 patients who developed ST segment changes. The results of London *et al.*,[15] while informative, should be interpreted with caution. The studies by Mason *et al.*[21] (56 patients) and Sketch *et al.*[22] (110 patients) are in subjects who were demonstrated to have angiographically proven coronary artery disease, making them similar to our study population. In these studies V_6 was as good as V_5. Whether patients with stable angina (such as those studied by London) have a different ECG response than those presenting for coronary artery surgery is not known. Certainly inclusion of patients with only risk factors makes it possible to have included patients without significant coronary artery disease. Also, the optimum lead for monitoring patients during and after sternotomy has not been determined. Variability in heart to chest wall relationships during cardiac surgery may make strict V_5 and V_6 distinctions less meaningful than we would like to believe. Thus, while of concern, we do not accept that the low sensitivity of V_6 found by London *et al.*[15] necessarily applies to patients undergoing coronary artery surgery, and await results of studies in this latter population.

Although lead II is considered desirable, adding this lead to four precordial leads increased sensitivity by only 2% in Blackburn's study, and 7% of patients in the study by Mason demonstrated ischemia in leads II or III alone. In the only study in anesthetized patients before that by London which reported the lead in which ischemia occurred, Coriat *et al.*[18] found that lead II never showed ischemia that was not also present on the precordial lead. In London's study although lead II alone showed a remarkable 33% sensitivity, it added only 5% to V_5. These studies[15,16,21] all found significant increases in sensitivity only with multiple precordial leads. Their findings suggest that any two-lead system using one precordial lead will miss at least 10% of ischemic episodes and probably 20–40%. We wish that we could report that V_9 (looking at the posterior LV wall and reflecting reciprocal changes of the anterior wall[23]) improved our sensitivity; however, like the findings of Coriat *et al.*[18] for lead II we never found ischemia on V_9 that was not already present on the precordial lead. Thus, apart from the question of V_6 raised in the study by London *et al.*,[15] it seems unlikely that the

sensitivity of our V_6 and V_9 system is much different from a V_5 equivalent combined with lead II.

Ischemic episodes occurred throughout the prebypass period in this study. One patient arrived in the operating room with ischemia (1%), which is strikingly different from the 18% incidence of preoperative ischemia reported by Slogoff and Keats[1] but similar to the 0% incidence reported by Knight *et al.* at this time.[19] Perhaps this is related to the use of diazepam for premedication in this study and in the study by Knight *et al.*[19] Thomson *et al.* have recently shown that compared with morphine and scopolamine, premedication with lorazepam results in decreased heart rate from the time of premedication in patients undergoing CABG surgery with fentanyl anesthesia.[24] Although we did not study this question, our results suggest that the addition of diazepam to morphine and scopolamine will result in a reduction in heart rate following premedication (table 2).

Only four of 16 episodes (25%) of ischemia occurred at induction or intubation in this study. This is similar to a previous study in which we found 50% of ischemic events to occur remote from induction and intubation.* Slogoff and Keats also found that ischemic events occurred throughout the prebypass period.[1] In contrast, Thomson has reported that ischemic events only occurred at induction and intubation and only in the presence of pancuronium, leading him to focus on the importance of the opiate–pancuronium combination, which may produce undesirable hemodynamics and result in ischemia.[2,13] Although abnormal hemodynamics, particularly tachycardia, are important in the genesis of myocardial ischemia, our results, similar to others[1,19] suggest that ischemia can occur in the presence of normal hemodynamics. Six of 16 episodes (37%) of ischemia occurred when there was no hemodynamic disturbance in this study, whereas Slogoff and Keats[1] reported a 50% incidence of "random ischemia" and Knight *et al.*[19] reported that only 42% of ischemic events occurred coincidently with a hemodynamic abnormality. Although it is difficult to reconcile the differences in the occurrence and timing of ischemia between this study and those of Thomson, important factors may be patient selection, sample size, anesthetic technique and management, and possibly the method used to detect ST segment changes. Computerized scanning of the Holter recordings, as used in this study, is a sensitive method to detect periods of ischemia of short duration.

The patients in this study received a standardized anesthetic technique. Premedication, which included a benzodiazepine, was followed by a moderate dose fentanyl induction with enflurane supplementation if needed for blood pressure control. This differs from other investigations of perioperative ischemia in which the anesthetic technique was uncontrolled[1,14,19] or a high-dose narcotic technique was used.[2,13,*] The effect of these various anesthetic techniques on the incidence of ischemia has not been studied; therefore, the results of this study may only apply to similiar patients receiving a similiar anesthetic.

Thirty-five per cent of the patients in this study received nitroglycerin sublingually or intravenously at some time during the prebypass period (with no difference between groups). Only five of ten patients in whom ischemia was identified retrospectively by the Holter received nitroglycerin intraoperatively. Despite a protocol to infuse nitroglycerin whenever ischemia was identified by the participating anesthesiologist, this was not done in five patients. This suggests that these episodes ranging from 2 to 15 min were missed, despite the monitoring of leads V_5 and II and the availability of a calibrated ECG printout. As recently demonstrated by London *et al.*[15] who reported that only 20% of ischemic episodes were recognized by the clinician, detection of a 1-mm ST depression on an oscilloscope screen may be difficult. Although a continuous paper printout might improve sensitivity, this would be impractical in most operating rooms. The use of a monitoring system with ST trending capabilities that continuously monitors the ST segment and displays a numerical value for the ST segment shift[25] may have resulted in all patients with significant ST changes being given nitroglycerin.

Four patients in this study developed a perioperative MI. The diagnosis of perioperative MI after CABG surgery is controversial, and several recommendations have been made with respect to the use of CPK-MB, ECG findings, and technetium pyrophosphate scans.[26–28] Our criteria of a CPK-MB greater than 60 IU and new ECG changes agrees with the diagnosis of definite or probable MI in other studies.[27,28] It is possible that because technetium pyrophosphate scanning was not used, an MI occuring in patients with ECG or CPK changes only may not have been diagnosed.[27]

In conclusion, if increased heart rate and changes in blood pressure are promptly treated, pancuronium or vecuronium can be used as the muscle relaxant with fentanyl for CABG surgery with a comparably low incidence of ischemia. Patients given pancuronium had significantly higher heart rates and cardiac indices at all times postinduction and required intraoperative beta blockade to control heart rates greater than 90 beats $\cdot$ min^{-1} significantly more often. The incidence of perioperative MI was 4% and could not be related to prebypass ischemia, but was associated with a significantly prolonged aortic crossclamp time.

References

1. Slogoff S, Keats AS: Does perioperative myocardial ischemia lead to postoperative myocardial infarction? ANESTHESIOLOGY 62: 107–114, 1985
2. Thomson IR, Putnins CL: Adverse effects of pancuronium during

high-dose fentanyl anesthesia for coronary artery bypass grafting. ANESTHESIOLOGY 62:708–713, 1985
3. Harrison L, Ralley FE, Wynands JE, Robbins GR, Sami M, Ripley R, Fullerton HA: The role of an ultra short-acting adrenergic blocker (Esmolol) in patients undergoing coronary artery bypass surgery. ANESTHESIOLOGY 66:413–418, 1987
4. Fahey MR, Morris RB, Miller RD, Sohn YJ, Cronnelly R, Gencarelli P: Clinical pharmacology of ORG NC45 (Norcuron™): A new nondepolarizing muscle relaxant. ANESTHESIOLOGY 55: 6–11, 1981
5. Cronnelly R, Fisher DM, Miller RD, Gencarelli P, Nguyen-Gruenki L, Castagnoli N: Pharmacokinetics and pharmacodynamics of Vecuronium (ORG NC45) and Pancuronium in anesthetized humans. ANESTHESIOLOGY 58:405–408, 1983
6. Morris RB, Cahalan MK, Miller RD, Wilkinson PL, Quasha AL, Robinson S: The cardiovascular effects of Vecuronium (ORG NC45) and Pancuronium in patients undergoing coronary artery bypass grafting. ANESTHESIOLOGY 58:438–440, 1983
7. Sethna DH, Starr NJ, Estafanous FG: Cardiovascular effects of non-depolarizing neuromuscular blockers in patients with coronary artery disease. Can Anaesth Soc J 33:280–286, 1986
8. Shanks CA: Pharmacokinetics of the non-depolarizing neuromuscular relaxants applied to calculation of bolus and infusion dosage regimens. ANESTHESIOLOGY 64:72–86, 1986
9. Barker GL, Briscoe CE: The Pathfinder High-Speed ECG Analyser. Br J Anaesth 53:1079–1082, 1981
10. Gravlee GP, Ramsay FM, Roy RC, Angert KC, Rogus AT, Pauca AL: A hemodynamic comparison of fentanyl, sufentanil, pancuronium and vecuronium. Anesth Analg 67:39–47, 1988
11. Reitan JA, Stengert KB, Wymore ML, Martucci RW: Central vagal control of fentanyl-induced bradycardia during halothane anesthesia. Anesth Analg 57:31–36, 1978
12. Ferres CJ, Carson IW, Lyons SM, Orr IA, Patterson CC, Clarke SJ: Hemodynamic effects of vecuronium, pancuronium and atracurium in patients with coronary artery disease. Br J Anaesth 59:305–311, 1987
13. Thomson IR, Mutch WAL, Culligan JD: Failure of intravenous nitroglycerin to prevent intraoperative myocardial ischemia during fentanyl-pancuronium anesthesia. ANESTHESIOLOGY 61: 385–393, 1984
14. Slogoff S, Keats AS: Does chronic treatment with calcium entry blocking drugs reduce perioperative myocardial ischemia? ANESTHESIOLOGY 68:676–680, 1988
15. London MJ, Hollenberg M, Wong MG, Levenson L, Tubau JF, Browner W, Mangano DT: Intraoperative myocardial ischemia: Localization by continuous 12-lead electrocardiography. ANESTHESIOLOGY 69:232–241, 1988
16. Blackburn H, Katigbak R: What electrocardiographic leads to take after exercise? Am Heart J 67:184–185, 1964
17. Thys DM, Kaplan JA: Recent advances in electrocardiographic techniques, Cardiac Anaesthesia, second edition, volume 1. Edited by Kaplan JA. Philadelphia, Grune & Stratton, 1987, pp 227–254
18. Coriat P, Daloz M, Bonssean D, Fusciardi J, Echter E, Viars P: Prevention of intraoperative myocardial ischemia during noncardiac surgery with intravenous nitroglycerin. ANESTHESIOLOGY 61:193–196, 1984
19. Knight AA, Hollenberg M, London MJ, Tubau J, Verrier E: Perioperative myocardial ischemia: Importance of the preoperative ischemic pattern. ANESTHESIOLOGY 68:681–688, 1988
20. Mason RE, Likar I: A new system of multiple-lead exercise electrocardiography. Am Heart J 71:196–205, 1966
21. Mason RE, Likar I, Biern RO, Ross RS: Multiple lead exercise electrocardiography. Experience in 107 normal subjects and 67 patients with angina pectoris and comparison with coronary cinearteriography in 84 patients. Circulation 36:517–525, 1967
22. Sketch MH, Nair CK, Esterbrooks DJ, Mohiuddin SM: Reliability of single-lead and multiple-lead electrocardiography during and after exercise. Chest 74:394–401, 1978
23. Friedman HH: Diagnostic Electrocardiography and Vectrocardiography, second edition. New York, McGraw-Hill, 1977, pp 246, 247
24. Thomson IR, Bergstrom RG, Rosenbloom M, Meatherall RC: Premedication and high dose fentanyl anesthesia for myocardial revascularization: A comparison of lorazepam versus morphine-scopolamine. ANESTHESIOLOGY 68:194–299, 1988
25. Kotrly KJ, Kotter GS, Mortara D, Kampine JP: Intraoperative detection of myocardial ischemia with an ST segment trend monitoring system. Anesth Analg 63:343–345, 1984
26. Graeber GM: Creatine kinase (CK): Its use in the evaluation of perioperative myocardial infarction. Surg Clin North Am 65: 539–551, 1985
27. Raabe DS, Morise A, Sbarbaro JA, Gundel WD: Diagnostic criteria for acute myocardial infarction in patients undergoing coronary artery bypass surgery. Circulation 62:869–878, 1980
28. Graeber GM, Shawl FA, Head HD, Wolf RE, Burge JR, Cafferty PJ, Lough FC, Zajtchuk R: Changes in serum creatine kinase and lactate dehydrogenase caused by acute perioperative myocardial infarction and by transatrial cardiac surgical procedures. J Thorac Cardiovasc Surg 92:63–72, 1986