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Postoperative Respiratory Care:

A Controlled Trial of Early and Late Extubation Following Coronary-artery Bypass Grafting

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Sequelae of early versus late extubation of the trachea in patients following coronary-artery bypass grafting were compared prospectively in 38 patients randomly assigned to one of the two groups. The times to extubation were 2 ± 2 and 18 ± 3 hours after operation for the two groups. Comparisons were made between groups for the following five variables: time spent in the intensive care unit; drug utilization in the intensive care unit; cardiopulmonary morbidity; hemodynamic performance; patient stress (plasma norepinephrine levels). The anesthetic technique consisted of induction with thiopental, nitrous oxide, and halothane, followed by maintenance with nitrous oxide and halothane. Pancuronium was the only muscle relaxant administered. Patients whose tracheas were extubated early had muscle relaxants reversed prior to the application of extubation criteria. There was no significant difference between the groups in times spent in the intensive care unit, hemodynamic performances, or plasma norepinephrine levels; however, the patients whose tracheas were extubated early received less morphine and diazepam and suffered significantly less cardiopulmonary morbidity. (Key words: Anesthetic techniques: extubation. Intensive care. Intubation, endotracheal: postoperative. Surgery, cardiac. Sympathetic nervous system: catecholamines, norepinephrine. Ventilation, mechanical.)

RECENT STUDIES SUGGEST that endotracheal extubation within several hours following uncomplicated coronary-artery bypass grafting (CABG) may accelerate recovery without increasing morbidity.[1,2] In addition to any possible effect on morbidity or rate of postoperative recovery, we questioned whether prolonged endotracheal intubation and controlled mechanical ventilation (CMV) would result in increased patient stress, with its attendant effects on hemodynamic performance. To our knowledge, no study had compared the hemodynamic and respiratory effects of early versus late extubation in these patients. We designed a prospective, randomized study to compare two groups of patients, those whose tracheas were extubated within eight hours following CABG and those whose tracheas were left intubated and whose lungs were mechanically ventilated overnight. The purpose of our study was to determine whether the duration of postoperative endotracheal intubation affected cardiopulmonary morbidity, hemodynamic performance, patient stress, drug utilization, or rate of recovery in the intensive care unit (ICU).

Methods

Informed, written consent, as approved by the University of California Committee on Human Research, was obtained from every subject on the evening prior to operation. Patients with normal or slightly impaired ventricular function undergoing elective CABG were selected (table 1). Bedside spirometry, ¶which included determinations of forced vital capacity and first-second forced expiratory volume (FEV_1/FVC), was performed on most patients the evening prior to operation for purposes of comparing pulmonary function between patient groups, but was not used as a criterion of selection. All patients were premedicated with morphine, 0.15 mg/kg, intramuscularly, diazepam, 0.15 mg/kg, orally, and either atropine or scopolamine intramuscularly. Prior to induction of anesthesia, peripheral intravenous and radial-artery catheters were placed using local anesthesia. With the patient supine and breathing room air, heparinized arterial blood (9 ml) was drawn for plasma norepinephrine[3] and blood-gas determinations. Results of control measurements of systolic, diastolic, and mean arterial pressures and heart rate were then recorded.

Anesthesia was induced with thiopental, nitrous oxide, oxygen, and halothane and maintained with nitrous oxide, oxygen, and halothane. Pancuronium was the only muscle relaxant administered. Following induction of anesthesia, a triple-lumen pulmonary-

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TABLE 1. Admission Criteria

1. Left ventricular end diastolic pressure (LVEDP) < 20 torr
2. Right atrial pressure (RAP) < 20 torr
3. Cardiac index (CI) > 1.9 l/min/m²
4. Ejection fraction (EF) > 0.40
5. Absence of new or uncontrolled arrhythmias
6. Absence of myocardial infarction within six weeks of operation

artery catheter** was placed via an internal jugular vein. Intraoperative monitoring included systemic and pulmonary arterial blood pressures (systolic, diastolic, and mean), pulse rate, electrocardiogram (V_5 lead), pulmonary capillary wedge pressure (PCWP), right atrial pressure (RAP), cardiac output, rectal and esophageal temperatures, urinary output, and serial arterial blood-gas measurements.

Cardiac output was determined at end-expiration using a thermodilution technique with 10 ml of iced saline solution and an Edwards 9520 computer.** All hemodynamic measurements throughout the study were done with the patient supine and undisturbed for at least 10 min. Arterial blood-gas values were analyzed using standard electrodes, which were calibrated before and after each determination. Saturations were calculated using a Severinghaus slide rule for samples obtained in the operating room and were measured directly with an IL CO-oximeter†† for samples obtained in the ICU. Intrapulmonary shunt was calculated at the termination of anesthesia while the patient's lungs were being ventilated with 100 per cent oxygen, by use of the standard equation.[4]

Hemodynamic values measured at the termination of anesthesia included cardiac output, systolic, diastolic and mean systemic and pulmonary arterial pressures, PCWP, RAP, and pulse rate. Plasma norepinephrine level was also determined at this time. Immediately prior to transport to the ICU, patients were randomly assigned to one of two groups (see below). All patients were taken directly from the operating room to the ICU, where their lungs were mechanically ventilated via the endotracheal tube with an MA1 ventilator‡‡ at a tidal volume of 15 ml/kg and respiratory rates sufficient to maintain arterial blood P_{CO_2} values between 35 and 40 torr. Patients in Group I had their lungs ventilated in this fashion until the following morning. Those in Group II were immediately assessed for hemodynamic and metabolic stability (table 2), and, once considered stable by these criteria, received reversal of muscle relaxants with neostigmine, 2.5 mg, and atropine, 1.0 mg, following which standard extubation criteria were applied (table 3). These extubation criteria were chosen because they comprised the routine criteria applied to patients following CABG at our institution. Patients in Group II had their tracheas extubated as soon as they met these criteria. When a patient did not meet the extubation criteria within eight hours of termination of the surgical procedure, the early-extubation attempt was considered a failure, and no further attempt to extubate the trachea was made until the following morning (7 AM), at which time the same extubation criteria were applied. Patients in Group I had identical stability and extubation criteria (tables 2 and 3) applied the morning (7 AM) of the first postoperative day. Hemodynamic measurements and plasma norepinephrine determinations were repeated four and eight hours postoperatively and at 6 AM on the first postoperative day. In addition, patients in Group I had an additional set of hemodynamic measurements and plasma norepinephrine determinations two hours after their late extubation.

All patients received morphine for analgesia and diazepam for sedation at the discretion of the house officer. Nitroprusside was used to control postoperative hypertension, defined as systolic blood pressure greater than 160 torr or diastolic pressure greater than 90 torr, or both, persisting despite apparently adequate analgesia and sedation.[5] Dopamine was the only drug used for inotropic support.

Groups I and II were compared with respect to the following: cardiovascular and pulmonary morbidity within 72 hours postoperatively; hemodynamic performance, which included systemic vascular resistance index, pulmonary vascular resistance

TABLE 2. Stability Criteria

1. Systolic blood pressure > 90 per cent of preoperative value
2. Chest tube output < 2 ml/kg/h
3. Pulmonary capillary wedge pressure (PCWP) and right atrial pressure (RAP) < 20 torr
4. Urinary output > 0.5 ml/kg/h
5. Temperature > 35.5 C
6. Arterial blood *p*H > 7.30
7. Absence of new or uncontrolled arrhythmias

TABLE 3. Extubation Criteria

1. Patient responsive to verbal stimuli
2. Maximum inspiratory force (MIF) > −20 cm H_2O
3. Vital capacity (VC) > 8 ml/kg
4. Alveolar–arterial oxygen tension difference < 400 torr at $F_{I_{O_2}}$ 1.0

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index, rate–pressure product and cardiac index obtained by use of standard equations; patient stress (plasma norepinephrine level); drug utilization (morphine, diazepam, nitroprusside, and dopamine) for total ICU stay, and length of stay in the ICU. Cardiovascular morbidity was defined as myocardial infarction, arrhythmias necessitating therapy, hypotension necessitating inotropic support, postoperative mediastinal hemorrhage necessitating surgical control, or cerebrovascular accident. Myocardial infarction was diagnosed by three physicians blinded to the study utilizing increases in myocardial enzyme values, positive technetium pyrophosphate scan, and electrocardiographic criteria (two definitely positive or one definitely positive and two questionably positive). Pulmonary morbidity was defined as pneumothorax, pneumonia, lobar collapse, or the need for reintubation of the trachea. For all patients, intrapulmonary shunt ($F_{I_{O_2}}$ 1.0) was calculated during CMV prior to extubation, and venous admixture ($F_{I_{O_2}}$ 0.4) was calculated two hours after extubation.[4] All mean drug dosages were calculated by dividing the total dosage received per patient by the total number of hours spent in the ICU by that patient.

Data between groups were compared by use of the Student *t* test for non-paired data and chi-square analysis, except for hemodynamic variables and plasma norepinephrine levels, which were analyzed using an analysis of variance with repeated measures. $P < 0.05$ was considered significant.

Results

Thirty-eight patients were studied. Twenty patients were randomized to Group I (late extubation), while 18 patients were randomized to Group II (early extubation). Of the 18 patients in Group II, 17 (94 per cent) met extubation criteria within the arbitrary cut-off period of eight hours following operation. One of the 17 early-extubated patients needed reintubation of the trachea two hours following extubation due to ventilatory failure (arterial blood *p*H 7.27, Pa_{CO_2} 56 torr).

TABLE 4. Pulmonary Classification

	Restrictive (Per Cent)	Obstructive (Per Cent)
Normal	FVC < 20 ↓	$FEV_1/FVC \geq 75$
Mild	FVC = 20–29 ↓	$FEV_1/FVC = 65–74$
Moderate	FVC = 30–40 ↓	$FEV_1/FVC = 55–64$
Severe	FVC > 40 ↓	$FEV_1/FVC < 55$

FVC = forced vital capacity.
FEV_1/FVC = first-second forced expiratory volume/forced vital capacity ratio.

Sixteen of the 18 patients (89 per cent) randomized for early tracheal extubation were therefore judged to represent extubation successes (Group IIS), whereas two patients (11 per cent) so randomized were judged to represent extubation failures (Group IIF). Groups I and IIS were similar with regard to age (60 ± 9 versus 56 ± 9 years), weight (77 ± 11 versus 73 ± 13 kg), and sex distribution. Groups I and IIS did not differ significantly with respect to preoperative ventricular function, as defined by LVEDP (11 ± 4 versus 11 ± 3 torr), RAP (6 ± 3 versus 7 ± 1 torr), cardiac index (2.7 ± .5 versus 2.4 ± .4 l/min/m²), and ejection fraction (.61 ± .16 versus .59 ± .11). Results of preoperative spirometry (FEV_1/FVC) were analyzed for both restrictive and obstructive patterns, which were then classified into normal, mild, moderate, and severe disease categories on the basis of the criteria listed in table 4. Using chi-square analysis, the two groups did not differ with respect to preoperative pulmonary function. Alveolar-to-arterial P_{O_2} differences during breathing of room air were similar for the two groups (18 ± 11 versus 24 ± 10 torr) prior to the induction of anesthesia, and intrapulmonary shunts ($F_{I_{O_2}}$ 1.0) were virtually identical in the two groups at the termination of anesthesia (22 ± 7 versus 21 ± 7 per cent). The two groups were similar with respect to intraoperative events, including number of vessels bypassed (2.4 ± .9 versus 2.3 ± .9), time of cardiopulmonary bypass (94 ± 33 versus 82 ± 30 min), and time of aortic cross-clamping (41 ± 17 versus 36 ± 18 min).

TABLE 5. Drug Requirements in the Intensive Care Unit

	Group I		Group II (Successful)		Group II (Failed)	
	$\bar{X} \pm SD$	Number of Patients/Total	$\bar{X} \pm SD$	Number of Patients/Total	$\bar{X}$	Number of Patients/Total
Morphine (μg/kg/h)	15 ± 6	20/20	9 ± 5*	16/16	10	2/2
Diazepam (ng/kg/h)	7 ± 5	13/20	2 ± 2	2/16†	3	1/2
Nitroprusside (μg/kg/min)	.5 ± 1	13/20	.2 ± .1	8/16	.1	2/2
Dopamine	—	1/20	—	0/16	—	0/2

* $P < .02$, Student *t* test compared with Group I for non-paired data.
† $P < .005$ compared with Group I, chi-square test.

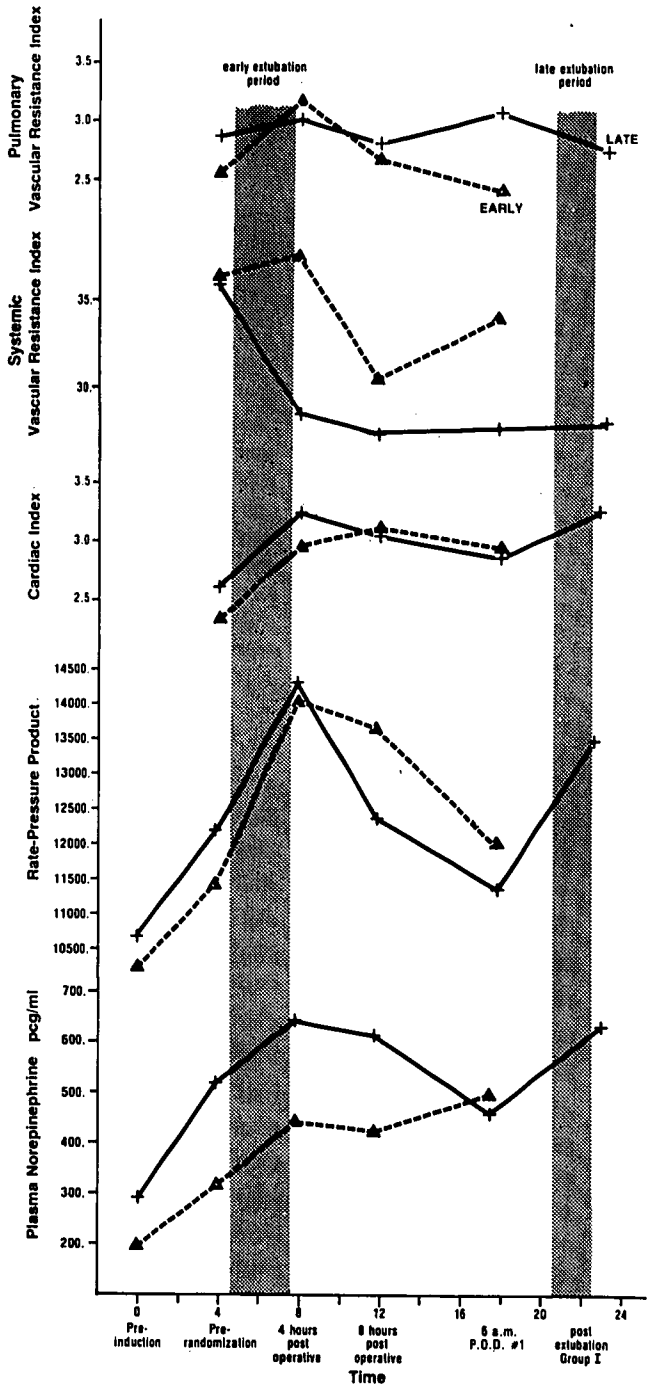

FIG. 1. Indices of hemodynamic performance and plasma norepinephrine level plotted against time. There was no significant difference between groups in any of the five study periods chosen. Patients whose tracheas were extubated late (18 hours) had an additional set of hemodynamic indices obtained two hours after tracheal extubation.

For the 16 patients whose tracheas were successfully extubated early (Group IIS), the average time to extubation was 2 ± 2 hours, compared with 18 ± 3 hours for Group I ($P < .001$). There was no significant difference between groups in length of time spent in the ICU, 46 ± 12 hours for Group IIS and 57 ± 29 hours for Group I.

Patients in Group I received 50 per cent more morphine ($P < .02$) and 400 per cent more diazepam than those in Group IIS (table 5). The requirements for nitroprusside were not significantly different between the two groups. Only one of 38 patients received dopamine during the ICU stay.

There were 13 morbid events in Group I: three myocardial infarctions; six patients with arrhythmias that necessitated therapy; two patients with lobar collapse; one patient who became hemiplegic on the second postoperative day due to a cerebrovascular accident and one patient with postoperative cardiac tamponade necessitating two reoperations. Four morbid events were documented in Group IIS: four patients with arrhythmias that necessitated therapy. One morbid event occurred in Group IIF, that is, the reintubation of the trachea. The total morbidity in Group I, 13 morbid events in 20 patients, was significantly greater than the morbidity in Group IIS, four morbid events in 16 patients; or Group IIS plus Group IIF (Group II), five morbid events in 18 patients.

The duration of CMV did not affect pulmonary gas exchange, since there was no difference between groups with respect to pre-extubation intrapulmonary shunt (19 ± 6 versus 20 ± 6 per cent) or postextubation venous admixture (17 ± 6 versus 17 ± 7 per cent). There was no significant difference between Groups I and IIS at any of the chosen study points (pre-induction control, prerandomization at the termination of anesthesia, four and eight hours postoperatively, and 6:00 AM on postoperative day 1) for cardiac index, systemic vascular resistance index, pulmonary vascular resistance index, rate–pressure product, or plasma norepinephrine level (fig. 1).

Discussion

In 1957, Bjork and Engstrom[6] reported the results of routine use of CMV for postoperative care of cardiac surgical patients. Spencer *et al.* described a series of seven patients who underwent open cardiac procedures, all of whom needed postoperative CMV for from one to seven days.[7] By 1966, five independent groups advocated routine CMV following cardiac surgery.[8–12] Peters *et al.*[13] and Thung *et al.*[14] demonstrated an increased work of breathing following cardiac surgical procedures. Andersen and Ghia measured increases in dead-space ventilation, total flow resistance, and alveolar–arterial oxygen tension differences, with corresponding decreases in total static chest-wall compliance, in postoperative cardiac

surgical patients.[15] It is noteworthy that all of the aforementioned studies involved patients who underwent open cardiac procedures only.

Midell *et al.*, in 1974, reported findings in 100 consecutive patients who underwent valve replacement, 90 of whose tracheas were extubated within several hours after operation.[16] None of their patients needed reintubation. Prakash *et al.*, in 1977, reported that following CABG procedures the tracheas of 56 of 62 (90 per cent) patients were successfully extubated, and noted that patients whose tracheas were extubated earlier needed fewer days of intensive care monitoring, without increased pulmonary morbidity.[1] Also in 1977, Klineberg *et al.* described the cases of 72 patients, 63 per cent of whom had successful tracheal extubation within five hours of arrival in the ICU.[2] Both Prakash[1] and Klineberg[2] and their co-workers concluded that earlier tracheal extubation permitted earlier patient mobilization without introducing additional morbidity. We questioned whether routine CMV was necessary for patients with normal or slightly impaired cardiac and pulmonary function undergoing elective CABG procedures, in view of the fact that these patients are distinctly different from those who underwent open cardiac procedures ten to 20 years ago.

The purpose of our study was to examine prospective early and late postoperative endotracheal extubation in two comparable groups of patients. We compared these two forms of therapy with regard to their effects on cardiopulmonary morbidity, rate of convalescence, drug utilization, patient stress, and hemodynamic performance. It is important to emphasize that all patients in our study received halothane–nitrous oxide anesthesia with reversal of muscle relaxants prior to extubation. Our conclusions cannot necessarily be extrapolated to patients receiving narcotic anesthetics.

Successful early extubation was accomplished in 16 of 18 patients (89 per cent). No morbidity other than that of one patient who needed reintubation was directly attributable to early extubation. It is unlikely that more stringent extubation criteria would have prevented the premature extubation of this patient, since his vital capacity was 15 ml/kg, maximal inspiratory force −40 cm H_2O, and intrapulmonary shunt 14 per cent prior to initial extubation. Immediately after extubation the patient complained of severe pain, and over the ensuing two hours he received morphine, 15 mg, intravenously, without adequate relief. Arterial blood-gas values were frequently monitored during this period, and progressively worsening respiratory acidosis was seen. Approximately three hours after tracheal extubation, the patient requested reintubation and to be "put to sleep." Four hours following initial extubation, after he had received morphine, 25 mg, intravenously, Pa_{CO_2} was 56 torr (arterial blood *p*H 7.27 and base excess −3). At this time the patient was still complaining of pain, and the trachea was electively reintubated using topical lidocaine anesthesia. Additional morphine, 10 mg, was administered intravenously over the next hour, and within two hours following reintubation the patient was asleep. The following morning, 12 hours after reintubation, identical extubation criteria (table 3) were applied, and the patient's trachea was successfully extubated following a 40-min trial of breathing via a T-piece circuit. It is likely that a trial of breathing via a T-piece circuit prior to initial extubation would have prevented the premature extubation of this patient's trachea but in view of his excellent pulmonary mechanics and gas exchange, this was not thought necessary. The one patient in Group II who failed to meet extubation criteria received the usual dose of morphine (10 mg, intravenously, over 10 hours) for patients in Group II in the immediate postoperative period, but was the only patient in Group II who received diazepam (10 mg, intravenously, over 10 hours) during the same period. The diazepam was administered by the attending house officer, who judged the patient to be unusually anxious. The extubation criteria that this patient failed to meet were numbers 1 though 3 in table 3, *i.e.*, his level of sedation may have been excessive.

Patients whose tracheas were extubated early (Group II) had a significantly lower incidence of combined early postoperative cardiopulmonary morbidity; however, no difference between groups was found for any of the individual morbid events (*i.e.*, myocardial infarction, lobar collapse, etc.). Indices of cardiopulmonary morbidity were chosen for their presumed relevance to prolonged CMV. We questioned whether a longer period of endotracheal intubation and CMV would result in an increased level of adrenergic stimulation (patient stress), manifested by higher levels of circulating norepinephrine, higher calculated vascular resistances and rate–pressure product (a reflection of myocardial oxygen consumption), or increased requirements for sedation, analgesia and nitroprusside. Plasma norepinephrine is a useful measure of stress if such variables as temperature, acid–base status and drug usage are controlled.[17] Thus, the stimulation of the surgical procedure, if not followed by continued patient stress, would not result in continued increases in postoperative norepinephrine levels. Cardiac index was measured in order to determine what effect any possible increase in adrenergic stimulation might have had on

cardiac function. To test any effect of adrenergic stimulation on cardiac morbidity, we chose reasonable indices of myocardial ischemia, *i.e.*, myocardial infarction, cardiac failure (hypotension necessitating inotropic support) and arrhythmias. We chose mediastinal hemorrhage and cerebrovascular accident as other reflections of hemodynamic stress (*i.e.*, hypertension). In an attempt to evaluate the pulmonary effects of early endotracheal extubation, we chose to compare indices of gas exchange prior to and two hours following extubation of the trachea, *i.e.*, intrapulmonary shunt and venous admixture, respectively. In addition, we examined the frequencies of occurrence of four common complications of CMV or premature endotracheal extubation, *i.e.*, pneumothorax, pneumonia, lobar collapse, and reintubation.

The incidence of myocardial infarction in the perioperative period following elective CABG procedures has been estimated to be between 10 and 15 per cent,[18] similar to our reported incidence of 8 per cent (three of 38 patients). We wondered whether the subgroup of three patients who had myocardial infarctions were different from other study patients with regard to hemodynamic variables or levels of stress. This was not the case. There was no difference in any of the measured or derived hemodynamic variables or plasma norepinephrine values that distinguished this subgroup from those patients who did not have perioperative myocardial infarction, regardless of whether they were compared with Group I, Group IIS, or the study group as a whole (Group I plus Group IIS). None of the myocardial infarctions proved to be hemodynamically significant, *i.e.*, resulting in a low-output syndrome, although one of the three patients was treated for continuous ventricular ectopic activity. Two of the myocardial infarctions occurred on the first postoperative day, while one occurred on the third postoperative day.

There was no difference between groups for any of the preoperative or postoperative indices of pulmonary function, despite the fact that two patients in Group I experienced lobar collapse in the immediate postoperative period. The lack of a significant difference between groups with regard to postoperative gas exchange may be explained by the relatively low incidence of this complication in Group I (two of 20 patients). It is possible that the presence of the endotracheal tube, which impaired the patient's ability to generate an effective cough, was partly responsible for the lobar collapse in two patients in Group I. The larger amounts of morphine and diazepam received by patients in Group I may have further contributed to the difficulty in clearing secretions.

The incidences of postoperative hypertension (*i.e.*, necessitating nitroprusside administration) in the two groups were not significantly different, nor were the amounts of nitroprusside utilized per patient. The overall incidence of hypertension in the immediate postoperative period in our patients was 61 per cent (23 of 38 patients), similar to previously reported incidences of 48 per cent,[19] 58 per cent,[20] and 59 per cent.[21] The presence of the endotracheal tube and CMV did not seem to have any significant effect on rate–pressure product, cardiac index, systemic vascular resistance index, pulmonary vascular resistance index, or plasma norepinephrine level.

Finally, early extubation did not significantly shorten the amount of time spent in the ICU. This was greatly affected, however, by intangibles such as ICU bed availability, surgical load, and the willingness of the surgical house officer to transfer the patient from the ICU to the ward. It was our clinical impression that patients whose tracheas were extubated earlier were mobilized earlier and could have been transferred to the ward earlier. Klineberg *et al.*[6] did, in fact, report that early extubation leads to earlier ICU discharge. The monetary savings for the early-extubation group amounted to $70.00 per patient, a small fraction of their total cost of hospitalization.

The relatively small number of patients studied precludes the conclusion that a cause-and-effect relationship exists between prolonged CMV with increased usage of sedatives and narcotics and increased cardiopulmonary morbidity following elective CABG procedures. In point of fact, the data do not elucidate the etiology of this difference in cardiopulmonary morbidity, since no difference was found in any of the hemodynamic or pulmonary indices chosen for examination. In addition, the data do not support the concept that prolonged CMV leads to an increased level of adrenergic stimulation, since plasma norepinephrine levels were similar in the two groups. However, this study does support the belief that prolonged CMV following CABG procedures should not necessarily be considered routine, and that early extubation of these patients' tracheas is safe provided that facilities for prompt reintubation are available. Further clinical studies are needed to establish the relative costs and benefits of using this approach.

In summary, early endotracheal extubation following elective CABG procedures was successful in 89 per cent of the cases, and was associated with less cardiopulmonary morbidity than was prolonged CMV when a halothane–nitrous oxide anesthetic technique was used. Sedative and narcotic requirements were less, but the ICU stay was not shortened by early extubation. The incidence of postoperative hypertension,

hemodynamic performance, and patient stress were not affected by early extubation. We conclude that early endotracheal extubation following uncomplicated CABG procedures with halothane anesthesia is safe and does not increase postoperative cardiac or pulmonary morbidity.

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