MORBIDITY OUTCOME IN EARLY VERSUS CONVENTIONAL TRACHEAL EXTUBATION AFTER CORONARY ARTERY BYPASS GRAFTING: A PROSPECTIVE RANDOMIZED CONTROLLED TRIAL

Davy C. H. Cheng, MD^a
Jacek Karski, MD^a
Charles Peniston, MD^b
Buvanendran Asokumar, MD^a
Ganesh Raveendran, MD^a
Jo Carroll, RN^a
Hillary Nierenberg, RN^a
Sandra Roger, RN^a
Don Mickle, MD^c
Jeff Tong, PhD^c
J. Zelovitsky, MD^d
Tirone David, MD^b
Alan Sandler, MB^a

Introduction: We undertook a prospective, randomized, controlled clinical trial to evaluate morbidity outcomes and safety of a modified anesthetic technique to provide shorter sedation and early extubation (1 to 6 hours) than those of the conventional anesthetic protocol used for prolonged sedation and extubation (12 to 22 hours) in patients after coronary artery bypass grafting. **Methods:** One hundred twenty patients undergoing elective coronary artery bypass grafting were prospectively assigned randomly to either an early extubation group ($n = 60$; $15 \mu\text{g} \cdot \text{kg}^{-1}$ fentanyl and 2 to 6 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{hour}^{-1}$ propofol and isoflurane) or to a conventional extubation group ($n = 60$; $50 \mu\text{g} \cdot \text{kg}^{-1}$ fentanyl and $0.1 \text{mg} \cdot \text{kg}^{-1}$ midazolam and isoflurane). Cardiac morbidity (postoperative myocardial ischemia, postoperative myocardial infarction, and perioperative sympathoadrenal stress response), respiratory morbidity (postextubation apnea, alveolar-arterial oxygen gradient, pulmonary shunting, oxygen consumption, atelectasis, and reintubation), hemodynamic values and vasoactive medication requirements, intraoperative awareness, postoperative cognitive function, 30 day mortality, and intensive care unit and hospital lengths of stay were compared between the two groups. **Results:** Fifty-one of the 60 patients in each group (85%) were extubated within the defined time period. Postoperative extubation time and intensive care unit and hospital lengths of stay were significantly shorter in the early group. At 48 hours after operation, there were no significant differences between the two groups in myocardial ischemia incidences, ischemia burdens, or creatine kinase isoenzyme MB levels. Four patients in the conventional group, but not in the early group, had postoperative myocardial infarction. The extubation anesthetics used were effective in suppressing the perioperative plasma catecholamine stress response in both groups. Postextubation apnea characteristics were similar between the groups. Intrapulmonary shunt fraction improved significantly in the early group at 4 hours after extubation. The incidences and degree of atelectasis did not differ significantly between the two groups. The incidences of treated postoperative complications were comparable between the two groups, but three patients in the conventional group died as a result of stroke or postoperative myocardial infarction. **Conclusion:** Early extubation after coronary artery bypass grafting is safe and does not increase perioperative morbidity. There is an improvement in postextubation intrapulmonary shunt fraction and a reduction in intensive care unit and hospital lengths of stay. (J Thorac Cardiovasc Surg 1996;112:755-64)

From the Division of Cardiac Anesthesia and Intensive Care, Department of Anaesthesia,^a and the Division of Cardiovascular Surgery, Departments of Surgery,^b Clinical Biochemistry,^c and Radiology,^d The Toronto Hospital, University of Toronto, Toronto, Ontario, Canada.

Received for publication Jan. 4, 1996; revisions requested Feb. 12, 1996; revisions received April 2, 1996; accepted for publication April 3, 1996.

Supported in part by a grant from the Anesthesia Patient Safety Foundation, American Society of Anesthesiologists, 1995, and by

an Investigator Award from the Society of Cardiovascular Anesthesiologists granted to Dr. Cheng, 1995.

Presented in part at the Canadian Anaesthetists Society Annual Meeting, June 1994, and at the American Society of Anesthesiologists Annual Meeting, Oct. 1994.

Address for reprints: Davy Cheng, MD, The Toronto Hospital, BW 4-646, 585 University Ave., Toronto, Ontario, Canada M5G 2C4.

Copyright © 1996 by Mosby-Year Book, Inc.

0022-5223/96 \$5.00 + 0 12/1/73913

The North American population is rapidly increasing in percentage of older persons, and the utilization of coronary artery bypass grafting (CABG) in the elderly population is doubling every 5 years.¹ The cost of morbidity and mortality after cardiac operations is inflated by increased severity of disease in patients undergoing CABG; these patients often are elderly, are undergoing extensive medical therapy, or have had previous angioplasty or revascularization.^{2,3} To diminish the escalating cost of cardiac operations, early postoperative tracheal extubation and discharge from the intensive care unit (ICU) have been advocated. To date, however, there have been insufficient data to ensure that morbidity outcome and quality of care for these patients are not compromised by early extubation. It should be noted that the economic consequences associated with post-CABG complications are far more costly than those of uncomplicated recovery.⁴

This prospective, randomized, controlled clinical trial was designed to evaluate the safety of a modified anesthetic protocol to provide shorter sedation and early extubation (1 to 6 hours) in patients after CABG, compared with that of the conventional anesthetic protocol for prolonged sedation and extubation (12 to 22 hours). Cardiac morbidity and perioperative sympathoadrenal stress response, respiratory morbidity, intraoperative awareness, postoperative cognitive function, and recovery were compared between the two groups.

Methods

Patient population. With the approval of the institutional Ethics Committee, 120 patients undergoing elective CABG were included in and consented to the study. Patients considered as study candidates were younger than 75 years, were scheduled for morning operation, were of either sex, had left ventricular function grades I through IV, and had either stable or unstable angina. Preoperative exclusion criteria were previous CABG or valvular heart operation, history of allergy to propofol or its constituents, left bundle branch block or current digitalis therapy, documented myocardial infarction (MI) within previous 3 weeks, active congestive cardiac failure, inotropic therapy within 24 hours before study onset or current intraaortic balloon pump support, severe hepatic disease (alanine aminotransferase or aspartate aminotransferase >150 IU/L), renal insufficiency (creatinine >180 $\mu\text{mol/L}$), severe chronic obstructive pulmonary disease (forced expiratory volume in 1 second <0.8 L), and history of seizure or stroke.

Study groups. Patients were randomly and consecutively allocated according to a computer-generated randomization code to early (study) or conventional (control) groups. Demographic data were recorded. Preoperative

sedation consisted of 1 to 3 mg sublingual lorazepam 1½ hours before the operation.

Early extubation group. Anesthesia induction consisted of 15 $\mu\text{g} \cdot \text{kg}^{-1}$ intravenous fentanyl $\pm$ 50 mg intravenous thiopental and 0.15 $\text{mg} \cdot \text{kg}^{-1}$ intravenous pancuronium for tracheal intubation. Anesthesia was maintained with 0.2% to 1.5% isoflurane and oxygen before cardiopulmonary bypass (CPB). No benzodiazepine was used. After initiation of CPB, propofol infusion at 2 to 6 $\text{mg} \cdot \text{kg}^{-1} \cdot \text{hour}^{-1}$ was commenced and maintained until 1 to 4 hours in the ICU. Postoperative sedation with propofol was adjusted to achieve a Ramsay sedation score of 3 to 4.⁵ Shivering was treated with 25 to 50 mg intravenous meperidine (Demerol). Persistent systemic hypertension (systemic blood pressure > 140 mm Hg) was treated with infusion of nitroglycerin, nitroprusside, or both, adjusted to achieve a systolic arterial pressure of 90 to 130 mm Hg. An intravenous bolus of 20 mg esmolol or 1 mg propranolol was used to control tachycardia (heart rate > 110 beats/min). A 50 to 100 mg indomethacin suppository was given for pain control at arrival in the ICU. Patients were assessed for tracheal extubation within 1 to 6 hours (Appendix 1). Analgesia was maintained after extubation by a 1 to 4 $\text{mg} \cdot \text{hour}^{-1}$ intravenous injection of morphine.

Conventional extubation group. Anesthesia induction consisted of 50 $\mu\text{g} \cdot \text{kg}^{-1}$ intravenous fentanyl and 0.15 $\text{mg} \cdot \text{kg}^{-1}$ intravenous pancuronium for tracheal intubation. A 0.1 $\text{mg} \cdot \text{kg}^{-1}$ intravenous injection of midazolam was administered in the prebypass period. Isoflurane (0.2% to 1.5%) was used as required during the peri-CPB period. In the ICU, routine infusions of morphine (2 to 10 $\text{mg} \cdot \text{hour}^{-1}$) and midazolam (1 to 3 $\text{mg} \cdot \text{hour}^{-1}$) were adjusted to achieve the same Ramsay sedation score. Treatments for shivering, hemodynamic parameters, and cardiac rhythm control were the same as in the early group. Sedation was discontinued the next morning, and a 50 to 100 mg indomethacin suppository was given for pain control. Patients were assessed for extubation at 7 AM, as in current conventional management.

Surgical procedure. All patients had radial and pulmonary arterial pressures monitored. Standard CABG was performed. Patients underwent a median sternotomy, with harvesting of saphenous veins and internal thoracic arteries as conduits. Myocardial protection was achieved with intermittent antegrade cold blood cardioplegic infusion through the aortic root, and the systemic temperature was allowed to drift down to 33° C during CPB. Hematocrit was maintained between 20% and 25% and CPB flow was maintained between 2.0 and 2.5 $\text{L} \cdot \text{min}^{-1} \cdot \text{m}^{-2}$. The mean perfusion pressure was kept at 50 to 60 mm Hg by adjustment of nitroprusside or phenylephrine infusion. Patients were actively rewarmed to 38° C before removal of the aortic crossclamp and weaning from CPB.

Outcome measurements

Cardiac morbidity

MYOCARDIAL ISCHEMIA. A clinically validated diagnostic electrocardiographic monitor (Mortara Instrument, Milwaukee, Wis.) for continuous real-time ST-segment analysis in 12 leads was used.⁶ The device, which compared samples to a baseline ST segment every 20 seconds, was attached to the patient 2 hours before operation. The

electrocardiogram was continuously monitored for 48 hours after operation. The incidence and severity of myocardial ischemia before and after extubation were compared within each group and between groups at each time interval. Myocardial ischemia burden was calculated from the area under the curve for the level and duration of ST-segment depression.

MI. Perioperative MI was diagnosed if either or both of the following findings were present: creatine kinase isoenzyme MB (CK-MB) concentration greater than 50 IU/L and representing more than 8% of total creatine kinase (CK) or major 12-lead electrocardiographic changes from baseline in two or more leads. Major 12-lead electrocardiographic changes were new Q waves of at least 0.04 seconds in duration and 1 mm in depth, ST-segment elevation or depression of greater than 2 mm lasting 48 hours, and a symmetric T-wave inversion persisting for 48 hours.^{7,8} Blood was analyzed for cardiac enzymes at 6, 12, 24, 36, and 48 hours after the release of the aortic crossclamp. Postoperative electrocardiogram was done daily for 3 days.

Catecholamine stress response. Plasma catecholamine levels (norepinephrine, epinephrine, and cortisol) were determined at baseline, 1 minute after intubation and sternotomy, 30 minutes after initiation of CPB, 15 minutes after arrival in the ICU, and 1 hour after extubation. Levels were assayed by high-pressure liquid chromatography.

Hemodynamic measurements. Heart rate, blood pressure, pulmonary artery pressure, central venous pressure, pulmonary capillary wedge pressure, cardiac index, cardiac output, systemic vascular resistance, and pulmonary vascular resistance were monitored and calculated at the following points: after induction, after intubation, after sternotomy, before CPB, after CPB, and hourly until 4 hours after extubation. Perioperative medications used were compared between the two groups.

Ventilatory morbidity

APNEA AND RESPIRATORY PATTERN. Respiratory inductive plethysmography is clinically validated and has proved reliable in critically ill patients.⁹ The Respitrace (Non-Invasive Monitoring Systems [NIMS], Miami Beach, Fla.) was recalibrated before extubation. After extubation, patients were continuously monitored for 4 hours. Breath-by-breath measurements of the following variables were recorded: respiratory frequency, inspiratory and expiratory times, tidal volume, inspiratory flow rate, minute ventilation, and percentage of rib cage or abdominal contributions to tidal volume. Central apnea was defined as an expiratory pause longer than 10 seconds or a tidal volume less than 100 ml. Obstructive apnea was defined as an expiratory pause longer than 10 seconds, negligible tidal volume associated with out-of-phase chest wall and abdominal movements, and a labored breathing index greater than 1.6. Ventilatory data were compared between the two groups.

ARTERIAL BLOOD GAS VALUES. Arterial blood gas values were measured at 5 minutes and 1, 2, and 4 hours after extubation.

ALVEOLAR-ARTERIAL OXYGEN GRADIENT. Alveolar-arterial oxygen gradient (A-aDo₂) was derived at 5 minutes after intubation and at 30 minutes and 4 hours after

extubation from the standard formula: $A-aDo_2 = PAO_2 - PaO_2$, where PAO_2 is alveolar oxygen tension and PaO_2 is arterial oxygen tension.

INTRAPULMONARY SHUNT AND OXYGEN CONSUMPTION. Both intrapulmonary shunt (Qs/Qt) and oxygen consumption ($\dot{V}O_2$) were calculated at 5 minutes after intubation and at 30 minutes and 4 hours after extubation from the standard formulas: $Qs/Qt = (Cco_2 - Cao_2)/(Cco_2 - C\bar{v}O_2)$ and $\dot{V}O_2 = CO(Cao_2 - C\bar{v}O_2)$, where Cco_2 is pulmonary capillary oxygen concentration, Cao_2 is arterial oxygen concentration, $C\bar{v}O_2$ is mixed venous oxygen concentration, and CO is cardiac output.

ATELECTASIS. Preoperative and postoperative chest roentgenograms were graded at 24, 48, and 72 hours after operation by a radiologist who was blinded to study group assignment.¹⁰

Awareness and cognitive function. Intraoperative awareness during the two anesthetic techniques was assessed by a standard questionnaire at 4 and 24 hours after extubation. The Mini-Mental State test was used to compare cognitive function before operation and 4 and 48 hours after extubation. This screening test combines a high validity and reliability with brevity and ease of application, avoiding fatigue in elderly subjects.¹¹

Other postoperative complications. Postoperative blood loss, shivering, reintubation, respiratory or cardiac arrest, and cerebrovascular accidents were recorded. Cerebrovascular accident was defined as the sudden onset of focal neurologic deficit, symptoms of focal neurologic deficit persisting longer than 24 hours, or both, as documented by a neurologist.

Mortality. Mortality was defined as any death occurring within 30 days after operation or during hospital stay.

Discharge criteria and actual discharge times. The discharge criteria were used to determine the time when the patient was medically fit to be discharged from either the ICU or hospital (Appendix 2). The actual discharge time was when the patient was actually discharged from either the ICU or hospital. The discharge criteria time provided a more valid and consistent comparison for postoperative recovery between the two groups than did the actual discharge time. Even though some patients were medically fit to be discharged from the ICU to the step-down unit on the same day, in practice they were not transferred out until the morning after the operation. Similarly, the actual discharge time from hospital was often longer than the time determined by discharge criteria because of social or home placement reasons.

Data collection and statistical analysis. Data for each patient were collected by a research nurse during the surgical course from hospital admission to discharge. Patients who did not fulfill the extubation criteria at the timed period were considered to have failure of extubation criteria. The reason for the failure was documented, and these patients were not excluded from statistical analysis. Because of failure of extubation, Respitrace data could not be collected. Myocardial ischemia and infarction data were collected and were included in the group comparisons.

The Clinical Trials Unit in the Center for Cardiovascular Research at The Toronto Hospital performed the biostatistical analysis. The distribution of each variable

Table I. Demographic data

	Early (n = 60)	Conventional (n = 60)
Age (yr)	59.3 ± 8.8	61.2 ± 8.7
Weight (kg)	79.5 ± 14.4	78.7 ± 13.7
Left ventricular grade (no.)	1.8 ± 0.9	1.8 ± 0.8
I	27	24
II	22	23
III	7	11
IV	4	2
No. of grafts per patients	3.7 ± 0.9	3.7 ± 0.9
CPB duration (min)	84.8 ± 28.3	86.8 ± 25.5
Crossclamp duration (min)	62.1 ± 19	64.1 ± 19.5

Table II. Postoperative recovery

	Early (n = 51)	Conventional (n = 51)
Extubation time (hr)	4.1 ± 1.1*	18.9 ± 1.4
ICU discharge criteria met (hr)	17.3 ± 12.1*	25.6 ± 12.3
Actual ICU discharge (hr)	29.2 ± 11.7	30.9 ± 12.8
Hospital discharge criteria met (days)	5.7 ± 2.4*	6.6 ± 2.4
Actual hospital discharge (days)	7.0 ± 2.5*	8.2 ± 3.5

**p* < 0.02

was examined, and significant variables were used for the outcome measurements. Discriminant function analysis was performed to ascertain whether a classification scheme developed and what variables contributed to group separation. Between-group comparisons of parametric data were assessed with unpaired *t* tests. A two-sided Fisher's Exact Test was used to analyze dichotomous frequency data. Serial comparisons of parametric data were analyzed by either a one-way analysis of variance or a two-way between-group analysis of variance with repeated measurements over time, followed by post hoc Scheffe's tests. All results were expressed as mean (± standard deviation).

Results

There were no differences in demographic data, including the distribution of left ventricular function, between the early and conventional groups (Table I). Fifty-one of 60 patients in the early group (85%) were extubated within the defined 6 hours after operation, and 51 of 60 patients in the conventional group (85%) were extubated within the defined 22 hours after operation. The postoperative extubation time and ICU and hospital lengths of stay were significantly shortened in the early group (Table II). There were nine patients (15%) in each group who did not meet

Table III. Extubation criteria failure

	Early (n = 9)	Conventional (n = 9)
Resternotomy (bleeding)	1	2
IABP or LCO syndrome	5	4
Inadequate ABGs	2	1
Reintubation (pneumonia)	1	0
CVA and death	0	2

IABP, Intraaortic balloon pump; LCO, low cardiac output; ABG, arterial blood gas values; CVA, cerebrovascular accident.

the extubation criteria within the defined time period, with comparable causes for failure (Table III).

Cardiac morbidity. No significant difference was found in postoperative myocardial ischemia incidence and ischemia burden between the two groups (Fig. 1). At arrival to the ICU, the incidence of myocardial ischemia was comparable between the early (35%) and conventional (31.7%) groups, decreasing in both to 16.7% after 4 hours. In the first 24 hours after operation, the ischemia incidence ranged from 13.3% to 20% in the early group and 5% to 16.7% in the conventional group; it progressively improved at end of 48 hours after operation to 6.7% in the early group and to 3.3% in the conventional group. In the first 24 hours after operation, myocardial ischemia burden appeared to be higher in the conventional group; on the second day after operation, however, myocardial ischemia burden tended to be higher in the early group. The mean duration of myocardial ischemia was 156.6 ± 143.2 minutes in the early group and 107.9 ± 119.5 min in the conventional group.

No significant difference was found between the two groups in CK-MB levels (Fig. 2), but total CK levels at 24 and 36 hours after operation were significantly higher in the conventional group. Four patients in the conventional group had postoperative MIs, and two of them died as a result of a difficult surgical graft. No postoperative MIs occurred in the early group.

Hemodynamic values and catecholamine stress response. Plasma catecholamine (norepinephrine, epinephrine, and cortisol) levels were all within the normal clinical range and did not differ significantly between the two groups (Fig. 3). There were no significant differences in perioperative hemodynamic values (heart rate, blood pressure, pulmonary artery pressure, central venous pressure, pulmonary capillary wedge pressure, cardiac index, cardiac output, systemic vascular resistance, and pulmonary

Fig. 1. Comparison of incidences of postoperative myocardial ischemia between early and conventional (Conv) groups through 48 hours.

vascular resistance) or in vasoactive medication requirements between the two groups.

Ventilatory morbidity. Postextubation oxygen saturation, respiratory rate, labored breath index (thoracoabdominal coordination), and apnea characteristics (Table IV) were similar between the two groups. Tidal volume (Fig. 4) and central respiratory drive improved with time in both groups. The early group had consistently lower minute ventilation and predominantly abdominal breathing after extubation. The incidence and degree of pulmonary atelectasis did not differ significantly between the two groups at 72 hours after operation.

There was no evidence of postextubation respiratory acidosis or hypoxemia in the early group when compared with the conventional group (inspired oxygen fraction 0.3). Qs/Qt was found to be significantly improved in the early versus conventional group at 4 hours after extubation (Table V).

Awareness and cognitive function. One patient in the early group reported awareness but no pain after CPB. One patient in the conventional group also reported awareness after operation, during transportation to the ICU. Although the difference was not statistically significant, the early group performed better and returned to baseline level earlier on the Mini-Mental State test than did the conventional group.

Postoperative complications. The incidences of postoperative treated complications were comparable between the two groups, as shown in Table VI. The conventional group had twice the incidence of

postoperative shivering (16.7%) seen in the early group (8.3%). Deaths occurred only in the conventional group; these three patients died of cerebrovascular accident and postoperative MI. The postoperative bleeding from chest tube drainage at 24 hours in the early group (548.2 ± 218.3 ml) was comparable to that in the conventional group (574.9 ± 255.3 ml).

Discussion

Although routine use of prolonged controlled ventilation in cardiac surgical patients has been standard practice for the past three decades, early tracheal extubation of these patients is not a new idea.^{12, 13} Cost containment and efficient resource use force the pendulum back to the debate of early extubation for cardiac surgical patients. Several groups have recently advocated early postoperative tracheal extubation and management of patients undergoing CABG in a cardiac recovery or step-down unit.¹⁴⁻¹⁶ Early extubation is now feasible because of improvement in anesthesia management coupled with advancements in surgical technique, myocardial protection, and postoperative hemostasis. The concept of balanced anesthesia rather than high-dose narcotics for cardiac operations has been reestablished.^{17, 18} Also, inhalational anesthetics such as isoflurane have been confirmed not to cause clinically significant coronary steal.^{19, 20} Specific postoperative sedation medications such as propofol are able to provide shorter postoperative sedation and time to extubation, with lower incidence of

Fig. 2. Comparison of postoperative CK-MB enzyme levels between the early and conventional (*Conv*) groups through 48 hours.

hypertension.^{21, 22} Morbidity and cost issues of early and late extubation for CABG have been raised and are still being debated.^{23, 24}

Cardiac morbidity. Perioperative myocardial ischemia has been shown to be associated with postoperative MI in patients undergoing cardiac operations.²⁵ Despite apparently successful revascularization, patients undergoing cardiac operations have had postoperative ischemia documented by continuous electrocardiography.²⁶ The peak incidence of ischemia (42% to 45%) was found within 2 hours after CPB and progressively reduced to less than 10% by 18 hours after CPB. Although intensive analgesia did not reduce postoperative MI rate, Mangano and coworkers²⁶ suggested that it is essential to reduce postoperative myocardial ischemia after CABG. The problem is that these patients would need to remain intubated and ventilated for 12 to 24 hours after the operation. The merit of our study is that it is the first prospective, randomized, comparative study of the effects of early versus conventional extubation on myocardial ischemia and MI. The incidences of myocardial ischemia were comparable in the early group (35%) and the conventional (31.7%) group, with both decreasing to 16.7% after 4 hours. In the first 24 hours after operation, the ischemia incidences ranged from 13.3% to 20% in the early group and from 5% to 16.7% in the conventional group; these progressively improved to 6.7% in the early group and 3.3%

in the conventional group at 48 hours after operation. Myocardial ischemia burden appeared to be higher in the conventional group during the first 24 hours after operation; on the second day after operation, however, it tended to be higher in the early group. We demonstrated no significant differences in postoperative myocardial ischemia incidence and ischemia burden between the two groups.

No significant differences in CK-MB levels were found between the two groups, but total CK levels were significantly higher in the conventional group at 24 and 36 hours after operation. Four patients in the conventional group had postoperative MIs, whereas no postoperative MIs occurred in the early group. Although the sample size in this study does not allow us to prove a significant reduction of postoperative MI with early extubation, the study does provide evidence that early extubation does not increase the risk of postoperative MI compared with conventional extubation.

Despite successful revascularization in patients having CABG, there is also a decrease in left ventricular ejection fraction compared with preoperative values.²⁷ It has been argued that a patient extubated in the first few hours after CPB might "look good" but have both functional and metabolic compromise of the myocardium.^{27, 28} Our data, with comparable demographic values including distribution of poor left ventricular function, indicate that early extubation anesthetic

Fig. 3. Comparison of perioperative catecholamine levels between the early and conventional (*Conv*) groups at baseline, 1 minute after induction, after sternotomy, 30 minutes into CPB, at ICU arrival, and 1 hour after extubation. *NE*, norepinephrine; *EP*, epinephrine.

management provides stable perioperative hemodynamic values without an increase in vasoactive medication requirement with respect to conventional management.

Sympathoadrenal stress. Cardiac operations present a specific problem because of the effects of hypothermic hemodilutional CPB on the activation of the sympathetic nervous system.²⁹ Epinephrine levels have been found to remain markedly elevated (300%) for 3 hours after arrival in the ICU. This suggests that the stress of CPB does not end with the operation. In an event comparison, our data demonstrate that the early extubation anesthetic protocol adequately suppressed the perioperative surgical and extubation stress response.

Respiratory morbidity. Prophylactic ventilation was championed in the early days of cardiac surgery to reduce the work of breathing with greater postoperative analgesia and promote better gas exchange.³⁰ More recent studies, however, do not support the use of prophylactic ventilation to prevent atelectasis. Dantzker and coworkers³¹ found no difference in Qs/Qt whether the patient was intubated or breathing spontaneously after CABG. A retrospective analysis of cardiac surgical patients revealed a higher incidence of postoperative atelectasis and longer ICU stays among patients in whom extubation was delayed beyond 24 hours.³² Quasha and colleagues¹³ reported an 89% success rate for early extubation and a lower incidence of lobar collapse in 18 patients undergoing CABG; they attributed these results to an improved ability to

Table IV. Postextubation apnea

	Early	Conventional
Incidence	27.5% (14/51)	33.3% (17/51)
Duration (sec)	17.7 ± 23.0	15.7 ± 28.6
Index (rate/hr)		
1 hr	13	15
2 hr	4	8
3 hr	2	9
4 hr	2	8

cough. Although some studies¹³⁻¹⁶ indicate that early extubation is possible or feasible in CABG, the incidence and outcome of respiratory complications (such as reintubation for respiratory failure, apnea, acidosis, and hypoxemia) after early extubation are not well documented. Prakash, Meij, and Van Der Borden³³ noted that the transition from controlled ventilation to either spontaneous or intermittent mandatory ventilation was associated with an increase in oxygen consumption and carbon dioxide production in patients undergoing CABG. Furthermore, Tulla and coworkers³⁴ suggested that return to spontaneous ventilation after cardiac operations was associated with increased work of breathing and risk of arterial hypoxia.

In our study, postoperative analgesia was provided by an indomethacin suppository before extubation. Unlike potent narcotics, this nonsteroidal anti-inflammatory drug has no respiratory depressive effect. Our data demonstrate that the respiratory mechanics after extubation were comparable

Fig. 4. Comparison of postextubation tidal volumes between the early and conventional (Conv) groups through 4 hours.

Table V. Postextubation arterial blood gas values

	Baseline		30 min		90 min		240 min	
	Early	Conventional	Early	Conventional	Early	Conventional	Early	Conventional
pH	7.41 ± 0.03	7.41 ± 0.03	7.36 ± 0.03	7.39 ± 0.03	7.37 ± 0.03	7.39 ± 0.04	7.37 ± 0.03	7.39 ± 0.03
Paco ₂	39.6 ± 4.2	38.9 ± 4.5	40.8 ± 4.8	39.3 ± 3.4	39.7 ± 4.5	39.5 ± 3.9	39.6 ± 4.3	39.6 ± 3.6
Pao ₂	140.9 ± 89.0	131.3 ± 73.4	142.5 ± 43.6*	125.2 ± 37.4	138.6 ± 37.4	125.7 ± 35.5	145.2 ± 48.8	129.9 ± 51.8
Vo	140.8 ± 50.9	139.6 ± 48.1	227.5 ± 74.9	214.1 ± 68.4	—	—	241.5 ± 115.6	206.6 ± 82.5
Qs/Qt	22.6 ± 10.6	20.3 ± 9.8	16.4 ± 13.6	21.5 ± 17.4	—	—	13.3 ± 9.2†	25.1 ± 24.1

Paco₂, Arterial carbon dioxide tension; PO₂, arterial oxygen tension.

*p < 0.035 between groups.

†p < 0.002 between groups.

between the two groups once the extubation criteria had been fulfilled. It did not matter whether the patients were extubated within a few hours or the next day after operation. The first hour after extubation is most crucial in respiratory care, as reflected by the apnea index. The tidal volume and central respiratory drive also improved progressively during the first hour after extubation. None of the early extubations resulted in respiratory acidosis, hypoxemia, or increase in postoperative pulmonary atelectasis. Early extubation improved Qs/Qt.

Postoperative recovery. There were nine patients in each group who could not be extubated in the prescribed time interval. The main reason was low cardiac output syndrome. In the early group, it was the result of temporary need of inotropic or intraaortic balloon pump support, whereas in the conventional group, it was the result of perioperative MI. As indicated in Tables III and VI, major

postoperative complications occurred mainly in the conventional group.

Clinically, the early group performed better and returned to baseline level earlier in the Mini-Mental test than did the conventional group. This allowed earlier chest tube removal, mobilization, and oral intake of food. The early group thus met discharge criteria for the ICU (17.3 hours vs 25.6 hours) and the hospital (5.7 days vs 6.6 days) much earlier than did the conventional group. In comparison, ICU length of stay averages from 2.3 to 5.2 days and hospital length of stay averages 13.9 days after CABG, as detailed in a multicenter study in Canada reported in 1993.³⁵

Conclusion

In this prospective, randomized, controlled clinical trial, our results indicate that early tracheal extubation of patients after CABG does not in-

Table VI. *Treated complications in the ICU*

	Early (n = 60)	Conventional (n = 60)
Seizure and stroke	0	2
Low cardiac output syndrome	7	8
Myocardial infarction	0	4
Arrhythmia	5	4
Reintubation	1	0
Bleeding	1	2
Low urine output	2	1
Shivering	5	10
Death	0	3

crease perioperative cardiac, respiratory, hemodynamic, or sympathoadrenal morbidity. It improves postextubation Qs/Qt and postoperative recovery, resulting in reduced lengths of stay in the ICU and the hospital.

We thank William Mahon, FRCPC, Peter Liu, FRCPC, and Richard Weisel, FRCSC (codirectors, Center of Cardiovascular Research [CCR]); Betty Ross (manager, CCR); and Peter Lewycky, PhD (biostatistician, CCR) for their advice in study design and statistical analysis. We thank Linda Jussaume, RN, and Doreen Craig, RN (managers, ICU); Ann Tattersall, RN, and Marion Ryu-jin, RN (managers, surgical ward); Jerry Hanimyan (director, Respiratory Therapy Department); Terry Hawn (Physiotherapy Department); and all the staff in the Divisions of Cardiac Anesthesia and Intensive Care and of Cardiovascular Surgery at The Toronto Hospital for their enthusiastic cooperation in this study.

REFERENCES

- Naylor CD, Ugnat AM, Weinkauf D, Anderson GM, Wielgosz A. Coronary artery bypass grafting in Canada: what is its rate of use? Which rate is right? *Can Med Assoc J* 1992;146:851-9.
- Weinstein MC, Coxson PG, Williams LW, Pass TM, Stason WB, Goldman L. Forecasting coronary heart disease incidence, mortality, and cost: the Coronary Heart Disease Policy model. *Am J Public Health* 1987;77:1417-26.
- Jones EL, Weintraub WS, Craver JM, Guyton RA, Cohen CL. Coronary bypass surgery: is the operation different today? *J Thorac Cardiovasc Surg* 1991;101:108-15.
- Taylor GJ, Mikell FL, Moses HW, Dove JT, Katholi RE, Malik SA, et al. Determinants of hospital charges for coronary artery bypass surgery: the economic consequences of postoperative complications. *Am J Cardiol* 1990;65:309-13.
- Ramsay MA, Savege TM, Simpson BR, Goodwin R. Controlled sedation with alphaxalone-alphadolone. *BMJ* 1974;2:656-9.
- Krucoff MW, Wagner NB, Pope JE, Mortara DM, Jackson YR, Bottner RK, et al. The portable programmable microprocessor-driven real-time 12-lead electrocardiographic monitor: a preliminary report of a new device for the noninvasive detection of successful reperfusion or silent coronary reocclusion. *Am J Cardiol* 1990;65:143-8.
- Lee TH, Goldman L. Serum enzyme assays in the diagnosis

of acute myocardial infarction: recommendations based on a quantitative analysis. *Ann Intern Med* 1986;105:221-33.

- Christakis GT, Ivanov J, Weisel RD, Birnbaum PL, David TE, Salerno TA, et al. The changing pattern of coronary artery bypass surgery. *Circulation* 1989;80(3 Pt 1):1151-61.
- Sackner MA, Krieger BP. Noninvasive respiratory monitoring. In: Scharf SM, Cassidy S, editors. *Heart-lung interactions in health and disease*. New York: Marcel Dekker, 1989:663-805.
- Seikaly H, Kuzon WM Jr, Gullane PJ, Herman SJ. Pulmonary atelectasis after reconstruction with pectoralis major flaps. *Arch Otolaryngol Head Neck Surg* 1990;116:575-7.
- Folstein M, Folstein S, McHugh P. Mini mental state: a practical method for grading the cognitive state of patients for the clinician. *J Psychiatr Res* 1975;12:189-98.
- Prakash O, Jonson B, Meij S, Bos E, Hugenholtz PG, Nauta J, et al. Criteria for early extubation after intracardiac surgery in adults. *Anesth Analg* 1977;56:703-8.
- Quasha AL, Loeber N, Feeley TW, Ulliyot DJ, Roizen MF. Postoperative respiratory care: a controlled trial of early and late extubation following coronary-artery bypass grafting. *Anesthesiology* 1980;52:135-41.
- Westaby S, Pillai R, Parry A, O'Regan D, Giannopoulos N, Grebenik K, et al. Does modern cardiac surgery require late intensive care? *Eur J Cardiothorac Surg* 1993;7:313-8.
- Chong JL, Grebenik C, Sinclair M, Fisher A, Pillai R, Westaby S. The effect of a cardiac surgical recovery area on the timing of extubation. *J Cardiothorac Vasc Anaesth* 1993;7:137-41.
- Engelman RM, Rousou JA, Flack JE, Deaton DW, Humphrey CB, Ellison LH, et al. Fast-track recovery of the coronary bypass patient. *Ann Thorac Surg* 1994;58:1742-6.
- Slogoff S, Keats AS. Randomized trial of primary anesthetic agents on outcome of coronary artery bypass operations. *Anesthesiology* 1989;70:179-88.
- Tuman KJ, McCarthy RJ, Spiess BD, DaValle M, Dabir R, Ivankovich AD. Does choice of anesthetic agent significantly affect outcome after coronary artery surgery? *Anesthesiology* 1989;70:189-98.
- Leung JM, Goehner P, O'Kelly BF, Hollenberg M, Pineda N, Cason BA, et al. Isoflurane anesthesia and myocardial ischemia: comparative risk versus sufentanil anesthesia in patients undergoing coronary artery bypass graft surgery. The SPI (Study of Perioperative Ischemia) Research Group. *Anesthesiology* 1991;74:838-47.
- Cheng DC, Moyers JR, Knutson RM, Gomez MN, Tinker JH. Dose-response relationship of isoflurane and halothane versus coronary perfusion pressures: effects on flow redistribution in a collateralized chronic swine model. *Anesthesiology* 1992;76:113-22.
- Chaudhri S, Kenny GN. Sedation after cardiac bypass surgery: comparison of propofol and midazolam in the presence of a computerized closed loop arterial pressure controller. *Br J Anaesth* 1992;68:98-9.
- Roekaerts PM, Huygen FJ, deLange S. Infusion of propofol versus midazolam for sedation in the intensive care unit following coronary artery surgery. *J Cardiothorac Vasc Anesth* 1993;7:142-7.
- Higgins TL. Pro: early extubation is preferable to late extubation in patients undergoing coronary artery surgery. *J Cardiothorac Vasc Anesth* 1992;6:488-93.
- Cheng DC. Pro: early extubation after cardiac surgery de-

- creases intensive care unit stay and cost. *J Cardiothorac Vasc Anesth* 1995;9:460-4.
25. Cheng DC, Chung F, Burns RJ, Houston PL, Feindel CM. Postoperative myocardial infarction documented by technetium pyrophosphate scan using single-photon emission computed tomography: significance of intraoperative myocardial ischemia and hemodynamic control. *Anesthesiology* 1989;71:818-26.
 26. Mangano DT, Siliciano D, Hollenberg M, Leung JM, Browner WS, Goehner P, et al. Postoperative myocardial ischemia: therapeutic trial using intensive analgesia following surgery. The Study of Perioperative Ischemia (SPI) Research Group. *Anesthesiology* 1992;76:342-53.
 27. Mangano D. Biventricular function after myocardial revascularization in humans: deterioration and recovery patterns during the first 24 hours. *Anesthesiology* 1985;62:571-7.
 28. Svedjeholm R, Ekroth R, Joachimsson PO, Ronquist G, Svensson S, Tydén H. Myocardial uptake of amino acids and other substrates in relation to myocardial oxygen consumption four hours after cardiac operations. *J Thorac Cardiovasc Surg* 1991;101:688-94.
 29. Okutani R, Philbin DM, Rosow CE, Koski G, Schneider RC. Effects of hypothermic hemodilutional cardiopulmonary bypass on plasma sufentanil and catecholamine concentrations in humans. *Anesth Analg* 1988;67:667-70.
 30. Thung NS, Norlander OP. Cardio-respiratory changes during anesthesia for open-heart surgery. *Acta Anaesthesiol Scand* 1966;10:79-110.
 31. Dantzker DR, Cowenhaven WM, Willoughby WJ, Kirsch MM, Bower JS. Gas exchange alterations associated with weaning from mechanical ventilation following coronary artery bypass grafting. *Chest* 1982;82:674-7.
 32. Ingersoll GL, Grippi MA. Preoperative pulmonary status and postoperative extubation outcome of patients undergoing elective cardiac surgery. *Heart Lung* 1991;20:137-43.
 33. Prakash O, Meij S, Van Der Borden B. Spontaneous ventilation test vs intermittent mandatory ventilation. *Chest* 1982;81:403-6.
 34. Tulla H, Takala J, Alhava E, Huttunen H, Kari A. Hypermetabolism after coronary artery bypass. *J Thorac Cardiovasc Surg* 1991;101:598-600.
 35. Mazer CD, Byrick RJ, Sibbald WJ, Chovaz PM, Goodman SJ, Girotti MJ. Postoperative utilization of critical care services by cardiac surgery: a multicenter study in the Canadian healthcare system. *Crit Care Med* 1993;21:851-9.

Appendixes

Appendix 1

Tracheal extubation criteria

- Patient responsive and cooperative
- Negative inspiratory force > -20 cm H₂O
- Vital capacity > 10 ml $\cdot$ kg⁻¹
- Arterial oxygen tension > 80 mm Hg, inspired oxygen fraction ≤ 0.5
- Cardiac index > 2.0 L $\cdot$ min⁻¹ $\cdot$ m⁻²
- Oropharyngeal temperature $> 36.5^\circ$ C
- pH > 7.30
- Chest tube drainage < 100 ml/hour $\times 2$ hours
- Absence of uncontrolled arrhythmia

Appendix 2

ICU discharge criteria

- Alert and cooperative patient
- No inotropic support and no significant arrhythmia
- Adequate ventilation (arterial oxygen tension > 80 mm Hg, arterial carbon dioxide tension < 60 mm Hg, arterial oxygen saturation $> 90\%$, inspired oxygen fraction ≤ 0.5 by face mask)
- Chest tube drainage < 50 ml/hour $\times 2$ hours
- Urine output > 0.5 ml $\cdot$ kg⁻¹ $\cdot$ hour⁻¹
- No active seizure

Hospital discharge criteria

- Hemodynamically stable
- Stable cardiac rhythm
- Noninfected incisions and afebrile patient
- Ability to void, bowel movements
- Independent ambulation and feeding