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Epidural Anesthesia and Analgesia in High-risk Surgical Patients

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The authors conducted a randomized controlled clinical trial to evaluate the effect of epidural anesthesia and postoperative analgesia (EAA) on postoperative morbidity in a group of high-risk surgical patients. A total of 53 patients were admitted to the study, 28 received EAA, and 25 received standard anesthetic and analgesic techniques without EAA. Surgical "risk" was evaluated preoperatively and found to be comparable in the two groups. When compared to control patients, patients who received EAA had a reduction in the overall postoperative complication rate ($P = 0.002$) and in the incidence of cardiovascular failure ($P = 0.007$) and major infectious complications ($P = 0.007$). Urinary cortisol excretion, a marker of the stress response, was significantly diminished during the first 24 postoperative hours in the group receiving EAA ($P = 0.025$). Finally, hospital costs were significantly reduced for patients who received EAA ($P = 0.02$). The authors conclude that EAA exerted a significant beneficial effect on operative outcome in a group of high risk surgical patients. (Key words: Anesthetic techniques: epidural. Narcotics: epidural. Surgery: postoperative morbidity.)

SHORTLY AFTER THE introduction of local anesthetics into clinical medicine proponants claimed that the use of regional anesthesia improved operative outcome.[1] Whether or not this is true has proven to be a remarkably difficult question to answer.

In recent years, regional anesthesia, and, in particular epidural anesthesia and postoperative analgesia (EAA), has been shown to exert a favorable effect on several aspects of operative outcome. These include a decrease in intraoperative blood loss,[2] postoperative catabolism,[3] and the incidence of thromboembolic events,[4] as well as improved vascular graft blood flow[5] and postoperative pulmonary function.[6,7] Several anesthetic techniques, including EAA, have also been shown to exert an inhibitory effect on the neuroendocrine response to the stress of an operation. The usual increase in plasma levels of the so-called "stress response" mediators such as adrenal steroids and catecholamines may be depressed by EAA.[8,9] We conducted a randomized, controlled clinical trial to compare EAA with general anesthesia and standard analgesic techniques in a select group of patients at high risk for postoperative morbidity. Our results indicate that some aspect of the anesthetic management of the patients who received EAA acted to improve their overall outcome.

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Materials and Methods

PATIENT SELECTION

Patients who met all the following criteria were considered eligible for entry into this study: (1) age greater than 18 years; (2) no contraindication to the insertion of an epidural catheter (localized infection, septicemia, preoperative coagulopathy); (3) scheduled for intrathoracic, intraabdominal, or major (non-cerebral) vascular surgery and; (4) scheduled preoperatively by the surgical staff to receive postoperative care in an intensive care unit (ICU) due either to the severity of pre-existing disease(s), the magnitude of the anticipated surgical procedure, or both. Those patients who met all of the above criteria and who gave informed, written consent were then randomized from a table of random numbers to receive either EAA as described below (group I) or a general anesthetic technique and parenteral narcotic administration for postoperative pain relief (group II). No attempt was made to alter the preoperative assessment or preparation of patients admitted to this study.

PERIOPERATIVE MANAGEMENT

Patients in both study groups received perioperative anesthetic care, including preoperative evaluation; choice of premedication, monitoring modalities, intraoperative anesthetic, and non-anesthesic agents; and immediate postoperative care which was under the direction of a staff anesthesiologist who was not one of the authors. Intraoperatively, patients in both groups were managed depending upon the patient's preoperative status and according to the usual dictates of good anesthesia care with provisions for patient amnesia, muscle relaxation, he-

modynamic stability, and optimal pulmonary function. In all patients in both groups, the trachea was intubated and ventilation was controlled for at least the duration of the operation. Patients in group I had a catheter placed preoperatively in the epidural space (usually in a low thoracic or high lumbar interspace depending upon the site of the surgical incision) to be utilized for operative anesthesia and postoperative analgesia.

Intraoperatively, patients in group I were maintained with light levels of general anesthesia, and received injections of local anesthetics in the epidural catheter of sufficient dose and concentration to achieve and maintain surgical anesthesia and muscle relaxation. Light general anesthesia was usually nitrous oxide, oxygen, and small dose of narcotics. Non-depolarizing muscle relaxants were frequently used for endotracheal intubation and control of ventilation, particularly during surgery of the upper abdomen and thorax. Local anesthetics used were either bupivacaine (0.75%) or lidocaine (1.5%) with epinephrine (1:200,000). Postoperatively, the physicians caring for patients in group I utilized the epidural catheter for pain relief using analgesic concentrations of local anesthetics and/or epidural administration of narcotics avoiding the use of parenteral narcotics for pain relief. The duration of postoperative epidural analgesia was a clinical decision not dictated by study protocol. Patients in Group II received either a high dose narcotic (defined as ≥35 μg/kg fentanyl with nitrous oxide, or ≥50 μg/kg fentanyl without nitrous oxide) or a "balanced" anesthetic technique. We defined balanced anesthesia as the administration of less than 35 μg/kg fentanyl or the equivalent dose of morphine (morphine:fentanyl equivalency ratio = 100:1) in combination with oxygen, a non-depolarizing muscle relaxant, and either nitrous oxide or a low concentration (≤1.0 MAC) of a potent inhalational anesthetic. Group II patients received postoperative parenteral narcotic analgesics, as required, for pain relief in the ICU, where one-on-one or one-on-two nursing assignments allowed for frequent evaluation of analgesic requirement and immediate administration of titrated doses of analgesics. Patients in both groups received "prn" parenteral or oral analgesics after discharge from the ICU. Routine intraoperative anesthesia monitors, such as continous electrocardiogram, indirect blood pressure determination, core temperature measurement, and measurement of inspired oxygen concentration, were utilized for all patients. In each case, the decision to utilize invasive hemodynamic monitoring was left to the attending anesthesiologist. All patients in both groups received postoperative intensive care, including continued hemodynamic monitoring and treatment, mechanical ventilation, and standardized nursing care protocols, as indicated. Patients remained in the ICU until the physicians caring for them felt that they could be transferred to a surgical ward. Except as noted, all aspects of perioperative care were under the direction of a staff surgeon or anesthesiologist, and were not dictated by study protocol.

Outcome Analysis

The physicians and nurses caring for patients in this study were not informed of the outcome variables under consideration. Major outcome variables selected for analysis were: (1) clinical outcome; (2) endocrine response; and (3) cost utilization.

Clinical outcome. Major clinical outcome variables analyzed were mortality and major morbidity. Mortality was defined as a death which occurred in the hospital while a patient was recovering from the original surgical procedure or a complication related to the original procedure. Major morbidity was defined as the appearance of organ failure, a major infectious complication (both as defined below), or re-operation for a complication related to the original surgical procedure (bleeding, infection, vascular by-pass occlusion).

Endocrine response. In all patients, urine was analyzed for free cortisol during an immediate preoperative period of approximately 2½ h (baseline), the intraoperative period, and during the first 2 postoperative days, or until the patient was discharged from the ICU. Baseline urine was collected *via* a urinary bladder catheter which was placed after anesthesia induction. Blood was drawn for analysis of serum cortisol during a baseline (immediately preoperatively) period, at 1 h after skin incision, and upon ICU arrival. These samples were kept frozen until analysis. Endocrine response was not analyzed in patients receiving steroid therapy.

Cost utilization. Variables analyzed for cost utilization were total anesthesia time, duration of postoperative endotracheal intubation (time until patients were first extubated), duration of postoperative stay in the ICU (time until patients were discharged from the ICU), duration of postoperative hospitalization, hospital costs incurred from the operative day until discharge (defined as the dollar amount for which the patient was billed, including charges for the hospital bed, operating room, respiratory therapy, materials services, pharmacy, laboratory, x-ray, and transfusion therapy), and physician charges incurred from the operative day until discharge (defined as the dollar amount for which the patient was billed, including charges for the original operation, x-ray interpretation, ECG interpretation, specialist consults, and critical care services).

Definitions

Because standardized definitions of postoperative morbidity and organ failure do not exist, the following definitions, used in this study, are presented. These def-

initions, prospectively identified, were based on our experience and the published experience of others which suggested that outcome is worse when one of these events is observed in the postoperative period. Particular emphasis is placed on the cardiovascular system.

Cardiovascular failure was defined as the appearance of one of the following in the postoperative period: transmural myocardial infarction (defined as the appearance on the electrocardiogram of new Q-waves at least 0.04 seconds in duration and 1 mm or more in depth); nontransmural myocardial infarction (diagnosed by a postoperative elevation of the serum lactate dehydrogenase and creatine phosphokinase, and by a creatine phosphokinase isoenzyme pattern considered to be diagnostic of myocardial damage with or without EKG changes); recent myocardial infarction diagnosed at autopsy; congestive heart failure (defined as the new appearance of classic chest x-ray changes and a pulmonary artery occlusion pressure (PAOP) greater than or equal to 20 mmHg, or one of the foregoing in conjunction with the new finding of rales on lung auscultation or an S3 gallop on cardiac auscultation); cardiogenic shock (defined as a cardiac index of less than $2\ l \cdot min^{-1} \cdot m^{-2}$ for more than 2 h, despite attempts at correction); ventricular tachyarrhythmia (defined as either documented ventricular tachycardia or fibrillation); supraventricular tachyarrhythmia (defined as the appearance of a new supraventricular tachyarrhythmia which required pharmacologic treatment due to concomitant evidence of myocardial ischemia, hypotension or a rapid ventricular response); heart block (defined as the new appearance of high grade atrioventricular block which required pacemaker placement); and angina (defined as the postoperative onset of either a new or unstable pattern of typical chest pain which the physicians caring for the patient felt to represent angina and which required pharmacologic therapy). Cardiovascular complications that appeared subsequent to a myocardial infarction were not considered as separate events.

Respiratory failure was defined as the need for mechanical ventilation for more than 24 h into the postoperative period, or the clinical decision to re-intubate and mechanically ventilate a patient who had been initially extubated postoperatively. The former definition was chosen to allow plasma levels of high doses of intraoperatively administered narcotic to fall below the threshhold for respiratory depression.[10] Renal failure was defined as a postoperative rise in the serum creatinine of more than 2 mg per deciliter. Gastrointestinal failure was defined as a gastrointestinal hemorrhage manifesting as the sudden appearance, unrelated to a surgical procedure, of frank blood either on nasogastric lavage or per rectum, with a subsequent fall in hemoglobin of 2 grams per deciliter or greater with no other known or suspected source of ongoing blood loss.

Pancreatic failure was defined as a new postoperative elevation of the serum amylase to twice the upper limits of normal in the absence of renal failure and recent upper abdominal surgery. Hepatic failure was defined as a new postoperative rise of the total bilirubin from a normal level to more than 5 mg per deciliter, and a rise of either the serum lactate dehydrogenase or aspartate transaminase to more than twice normal in the absence of upper abdominal surgery. A major infection was defined as the development of either pneumonia or sepsis. Pneumonia was defined as the new appearance of an infiltrate on chest x-ray and the new finding of 2 of 3 clinical criteria (temperature of 38° C or more, an abnormal elevation of the white blood cell count, or a sputum gram stain and culture positive for a pathogen). Sepsis was defined by the presence of a localized infection with a culture positive for a pathogen and 1 of 3 other possible clinical or laboratory criteria: 1) a positive blood culture for the same localized pathogen; 2) clinical evidence of bacteremia with chills, rigors, fever, and an elevated white blood cell count; or 3) hemodynamic evidence of sepsis with high cardiac output and low total peripheral resistance, accompanied by fever and an elevated white blood cell count.

Duration of Effective Catheter Use

In group I, the duration of effective epidural catheter use was defined as follows: if only analgesic concentrations of local anesthetic were utilized, the duration of effective catheter use was the time from the end of the surgical procedure until the use of parenteral narcotic analgesics was initiated. If epidural narcotic medications were utilized for pain relief, the duration of effective catheter use was defined as the time from the end of the surgical procedure, until either the initiation of parenteral narcotic analgesic medications, or until 8 h after the last dose of epidural narcotic medication was given. Patients in the epidural group who never required parenteral narcotics were not included in this analysis.

Cortisol Assay

Cortisol was determined by solid phase radioimmunoassay as described previously,[11] based on procedures developed by Ruder *et al.*[12] and Catt.[13] The materials used were supplied in kit form by Clinical Assays of Travenol-Genentech Diagnostics, and allowed for assay of both plasma cortisol and urinary free cortisol. Sensitivity of this assay is 24 pg of cortisol or 0.24 μg/dl. Results of analysis for interassay precision, based on 58 separate assays of a control sample, were a mean of 1.71 ng and a coefficient of variation of 5.5%.

TABLE 1. Patient Characteristics

	Group I (n = 28)	Group II (n = 25)	*P* Value
ASA physical status classification	2.79 ± 0.55	2.78 ± 0.78	N.S.
Goldman Index	9.1 ± 6.8	7.3 ± 3.9	N.S.
Age (yr)	71.2 ± 10.0	71.5 ± 7.7	N.S.
Type of operation*			
Intra-abdominal	13	11	N.S.
Intra-thoracic	5	2	N.S.
Major Vascular	10	12	N.S.
Baseline serum cortisol (μg/dl)	13.4 ± 5.1	16.8 ± 10.7	N.S.
Baseline cortisol excretion rate (μg/hr)	10.3 ± 5.5	21.6 ± 23.6	N.S.

N.S. = Not significant. Data are mean ± standard deviation.
* Reported as number of patients.

STATISTICAL METHODS

Standard methods were used to assess statistical significance, including the two-sample *t* test, the chi-square test, and Fisher's Exact Test for 2 × 2 tables. Measurements with skewed distributions were transformed using natural logarithms (and, optionally, scale shifts when values were negative) to achieve approximate Gaussianity. Patients with a value missing on a given clinical parameter were dropped from a particular comparison. In general, all patients who were randomized and received surgery were included in the statistical comparisons; exceptions are individually indicated in the text. Postoperative mortality and morbidity events in the two groups were compared using Fisher's Exact Test. All *P* values are two-sided. Significance was assessed at the 0.05 level.

This study was approved by the Dartmouth-Hitchcock Medical Center Institutional Review Board.

TABLE 2. Postoperative Morbidity and Mortality

	Group I	Group II	*P* Value*
Mortality	0	4	0.04
Morbidity:			
Cardiovascular failure	4	13	0.007
Respiratory failure	3‡	8	N.S.
Renal failure	1	3	N.S.
Hepatic failure	1	2	N.S.
Pancreatic failure	0	0	N.S.
Gastrointestinal failure	0	1	N.S.
Major infections	2	10	0.007
Re-operation	1	3	N.S.
Complication rate†	9/28	19/25	0.002

N.S. = Not significant
* *P* value from Fisher's Exact Test (two-sided).
† Number of patients with one or more complications.
‡ Two of three patients had a non-functioning epidural catheter. If this subgroup is excluded from the analysis, the *P* value is 0.009.

Results

PATIENT POPULATION

A total of 55 patients were enrolled in this study, 28 in group I, and 27 in group II. Surgery originally scheduled for two patients in group II was canceled after they were randomized. These two patients were eliminated from the study. The remaining 53 patients comprised the total patient population studied. The preoperative assessment (American Society of Anesthesiologists' Physical Status,[14] Goldman Index[15]) and characteristics of the two groups are presented in table 1. The study groups are comparable based on these criteria. One patient in each group was receiving long-term steroid therapy.

PERIOPERATIVE MANAGEMENT

Monitoring. All patients except one in group I were monitored with continuous intra-arterial pressure monitoring. Seventeen patients in group I and 21 patients in group II underwent preoperative pulmonary-artery catheterization.

Anesthetic management. All patients in Group I received a light general anesthetic, which was usually nitrous oxide with small supplemental doses of either a narcotic or a potent inhalational agent. Three patients in group I did not have a functioning epidural catheter; one, due to technical failure, and two, because a catheter was never inserted by independent decision of the anesthesiologist in charge of the case. Seventeen patients in group II received a high-dose narcotic anesthetic, and eight received a balanced anesthetic technique.

Duration of effective catheter use. In group I, 24 of the 25 patients with a functioning epidural catheter received epidural narcotics for pain relief. One patient received local anesthetic medications only for maintenance of epidural analgesia. The average duration of catheter use for postoperative analgesia was 31 h (range: 8–79 h). Two patients in group I, undergoing abdominal surgery, never required parenteral analgesics after the administration of epidural narcotics.

OUTCOME ANALYSIS

Patients in group I without a functioning epidural catheter are included for analysis with all other group I patients. This is done in order to maintain the value of the original randomization sequence. We view these patients as "treatment failures."

Clinical outcome. In group I, 9 of 28 patients developed one or more postoperative complications, compared to 19 of 25 patients in group II (table 2). Of the patients who developed postoperative complications, those in group I developed approximately half as many as those

in group II (12 in 9 patients *vs.* 49 in 19 patients, respectively) (table 3). If one excludes from group I those patients without a functioning epidural catheter, the group I complications rate is seven out of 25 patients, and the total number of complications is nine in seven patients. Statistical significance for all outcome variables was not altered by including data from the three patients with "nonfunctioning" epidural cathers in the group I data. This is true except for the incidence of respiratory failure, which would achieve statistical significance at the $P = 0.009$ level if these three patients were excluded from the analysis. There were no deaths in the group I patients. There were four deaths in group II patients on postoperative days 13, 17, 18, and 37. Complications were distributed evenly between all three categories of operative procedures (table 4).

Endocrine response. The results of the analysis of serum cortisol and urinary free cortisol excretion are presented in table 5. Patients in group I had a significantly reduced rate of cortisol excretion for the first 24 postoperative hours, which approximates the average duration of postoperative epidural analgesia. This significant difference in the rate of urinary cortisol excretion disappeared during the second 24 postoperative hours.

Cost utilization. The results of the analysis of the cost-utilization variables are presented in table 6. Group I patients spent an average (mean) of 6.1 h (range: 0–39 h) receiving postoperative mechanical ventilation, compared to an average (mean) of 81.8 h for group II patients (range: 0–840 h) ($P < .005$). Sixteen group I patients were ventilated for less than 2 h in the postoperative period, compared to two patients in group II who required less than 2 h of postoperative mechanical ventilation. The average hospital cost for group I patients ($11,218; range: $3,600–$32,700) was also significantly less than the average cost for group II patients ($20,380; range: $5,000–$95,000). The average physician costs for group I patients ($3,801; range: $1,080–$7,050) was less than group II patients ($5,134; range: $1,840–$13,770). Although group I patients spent, on average, fewer days in the ICU and fewer days in hospital postoperatively, these differences were not statistically significant, due partly to a wide range of ICU and hospital days for group II patients (0.21–42 days in ICU, 6–62 days in hospital) compared to group I patients (0.21–8 days in ICU, 5–21 days in hospital).

TABLE 3. Overall Morbidity

	Group I	Group II
Cardiovascular failure		
Myocardial infarction*	0	3
Congestive heart failure†	1	10
Ventricular tachyarrythmia	1	0
Supraventricular tachyarrythmia	2§	4
Angina	0	1
Heart block	0	1
Respiratory failure		
Prolonged ventilation	1§	6
Re-intubation	2§	2
Renal failure	1	3
Hepatic failure	1	2
Pancreatic failure	0	0
Gastrointestinal failure	0	1
Major infections		
pneumonia	1	9
sepsis	1	4
Re-operation	1	3
Total	12	49
Complication Intensity‡	12/9	49/19 $P = 0.004$

* Two non-transmural and one autopsy proven myocardial infarction.

† An S3 gallop was not a diagnostic criterion for any patient who developed congestive heart failure.

‡ Total number of complications observed divided by the number of patients who had one or more complications.

§ One each of these complications were in patients with a non-functioning epidural catheter.

Discussion

"Multiple system failure" is the term used to describe and organize the physiologic abnormalities observed in critically ill patients. Because patients entered in this study were anticipated to manifest characteristics of the critically ill, we organized our analysis of operative outcome with an emphasis on recognition of organ system failure. Although exact definitions may vary, the importance of organ failure can be recognized in the common assessment, expressed by Tilney, that "failure of one system challenges others," and does so by one of two basic mechanisms.[16] The first is the primary physiologic effect or effects of isolated organ failure, which is magnified by the consequent dysfunction of other systems. The second mechanism is the effect of therapy, which is frequently organ-specific and exerts detrimental side effects. These interactions are quite complex and, in the patient with multiple system failure, cause often becomes so indistinguishable from effect that therapy is simply goal-directed, aimed at interrupting the cyclic deterioration of interdependent organ systems. Epidural anesthesia and analgesia, which has multiple and potentially beneficial physiologic effects,

TABLE 4. Morbidity

Type of Operation	Group I (n)	Group II (n)
Intraabdominal	7 (13)	16 (11)*
Intrathoracic	2 (5)	5 (2)
Major vascular	3 (10)	28 (12)*

* = mortality

TABLE 5. Serum and Urine Cortisol

	Group I (n)	Group II (n)	*P* Value
Serum cortisol (μg/dl)*			
1 h after incision	12.6 ± 11.3 (20)	17.7 ± 19.2 (21)	N.S.
ICU arrival	14.6 ± 8.3 (19)	16.2 ± 14.5 (16)	N.S.
Urine cortisol excretion rate (μg/hr)*			
Total 1st 24 h	37.2 ± 27.0 (16)	73.8 ± 61.9 (13)	0.025
Total 2nd 24 h	34.9 ± 58.0 (7)	30.3 ± 45.4 (8)	N.S.

N.S. = Not significant. Data are mean ± standard deviation.
* Expressed as excess above baseline.

may be of benefit in the prevention of single or multiple system failure.

Postoperative respiratory failure, defined here as the requirement for mechanical ventilation, has numerous causes, some of which have been previously shown to be favorably affected by EAA. When compared to other analgesic techniques, the use of EAA has been associated with less sedation,[17] earlier ambulation,[6,18] higher pulmonary flow rates,[6,19] and improved oxygenation,[7,17,20,21] in the postoperative period. In the present study, patients who received EAA also had a reduction in the overall postoperative complication rate for other events which clearly compromise pulmonary function, such as pneumonia and congestive heart failure. Since an S3 gallop was not recorded as a diagnostic criterion for any episode of congestive heart failure, then, by our definition, all patients with congestive heart failure had evidence of pulmonary fluid overload, either on chest x-ray or physical examination (rales). Patients who received EAA also had a decreased incidence of events which affect pulmonary function less directly, such as renal failure with volume overload. Although, as expected, we could not define a precise etiology for each episode of respiratory failure, organ system interaction was evident. That is, patients who received standard anesthetic and analgesic techniques had the higher incidence of both respiratory and non-respiratory complications. Patients who received EAA had the lower incidence of respiratory and non-respiratory complications. Thus, EAA exerts multiple beneficial effects in high-risk surgical patients, including earlier return of consciousness and adequate spontaneous ventilation, less sedation, and, in our study, was associated with fewer non-pulmonary complications. All of these effects decrease the requirement for postoperative mechanical ventilation.

TABLE 6. Postoperative Cost Utilization

	Group I	Group II	*P* Value
Anesthesia time (h)	5.75 ± 1.71	6.47 ± 2.02	N.S.
Intubation (h)	7.1 ± 10.1	81.8 ± 186.1	0.005
ICU stay (days)	2.5 ± 1.8	5.7 ± 9.3	N.S.
Hospital stay (days)	11.4 ± 4.6	15.8 ± 12.3	N.S.
Hospital cost ($)	11,218 ± 5,738	20,380 ± 20,343	0.02
Physician cost ($)	3,801 ± 1,342	5,134 ± 2,939	0.05

P value (two sided) based on two-sample *t* test; transformation of measurement scale using natural logarithms to correct for skewed distributions. N.S. = Not significant. Data are mean ± standard deviation.

The cardiovascular effects of intraoperative epidural anesthesia in healthy subjects are well defined and usually minimal,[22] while the effects in patients with pre-existing cardiovascular disease may be significant. Recent investigations in patients with known cardiovascular disease have shown that, when compared to neurolept anesthesia, EAA is associated with more stable intraoperative hemodynamics with fewer episodes of myocardial ischemia.¶ The mechanisms involved are thought to include afferent sensory blockade, decreased adrenergic tone, and coronary and systemic vasodilation with a reduction in cardiac preload and afterload.[9,23,24] In the present study, the apparent benefit of EAA appeared during the postoperative period, when the effects of EAA on cardiovascular performance have not been well described. Epidural analgesia has been shown to be a very effective technique for relieving postoperative pain by blocking afferent nociceptive stimuli.[25] However, adrenergic tone, as assessed by plasma catecholamines and urinary catecholamine excretion, does not appear to be consistantly diminished by postoperative use of EAA. Some investigators have reported a decrease in postoperative plasma catecholamines,[26] while others have not documented this by a reduction in catecholamine excretion.[27] The effect of postoperative EAA on myocardial preload and afterload has not, to our knowledge, been previously studied.

We found that patients who received EAA had a reduced incidence of cardiovascular complications, including congestive heart failure, which means that abnormal elevations of left ventricular preload were less likely to occur in this group. All other types of cardiovascular failure were also less frequent in this group, but the mechanisms involved were not defined in this study. Finally, EAA may have indirectly benefited the cardiovascular system by reducing the incidence of non-cardiovascular complications. We cannot, therefore, ascribe the reduced cardiovascular morbidity in group I patients to any single, specific effect of EAA. It appears to result from improved pain control, venodilation with fewer abnormal elevations of cardiac preload, a lessened overall complication rate, and, possibly, other factors yet to be defined.

At least three lines of evidence, extant and here presented, indicate that utilization of EAA in this study acted

¶ Reiz S, Balfors E, Sorensen MB, Haggmark S, Nyhman H: Coronary hemodynamic effects of general anesthesia and surgery, Symposium: Influence of Anaesthetic Procedures on Surgical Sequelae. Edited by Carron H, Covino BG. Reg Anes 7 (suppl):S8–S18, 1982.

directly to diminish the incidence of major infectious complications in the postoperative period. First, patients who received EAA had a decreased duration of endotracheal intubation and mechanical ventilation, which have been shown to diminish many of the lung's defense mechanisms against infection.[28,29] Second, since our definition of sepsis was an event associated with infection at a primary locus, does EAA act to diminish the incidence of primary infections? Previous workers have suggested a decreased incidence of bowel anastomotic dehiscence after spinal anesthesia or EAA,[30] and we found a decreased incidence of pneumonia, both of which can act as a bacterial source for septicemia.[31,32] In addition, the fact that the patients in group II spent, on average, more time in the ICU postoperatively indicates a more prolonged duration of invasive monitoring and risk of nosocomial infection.[33,34] Finally, a well documented component of the stress response in humans is an inhibition of the immune system.[35] Our results, which are in general agreement with previous studies,[36] demonstrate a diminution of the stress response in patients who received EAA. This suggests that immunocompetence would be better maintained in this group. In fact, several investigators have demonstrated an improvement in some markers of postoperative immunocompetence when EAA is compared to other anesthetic and analgesic techniques.[37,38]

The overall complication rate and complication intensity were strikingly higher in group II patients. It was due to this fact that we felt it necessary to terminate our study. Despite the statistical significance of these findings, we believe that care should be taken in interpreting the difference in mortality between the two groups. This is particularly important because the number of observed events (deaths) were few and the study groups were relatively small.

Finally, concerns which center on issues of health care costs and utilization of hospital services are now prevalent in most medical communities. Although our primary concern must remain with patient well-being, there is also no doubt that morbidity is expensive,[39] and any intervention which reduces morbidity may also be expected to reduce health care costs. Our results agree with this conclusion. That is, the group II patients who had the higher morbidity also had the higher hospital and physician charges.

In summary, we believe our results confirm that techniques chosen to provide perioperative anesthesia and analgesia have a significant effect on postoperative events. In addition, the use of EAA in a group of high risk surgical patients is associated with decreased postoperative morbidity and improved operative outcome.

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