Postoperative Pulmonary Complications

Epidural Analgesia Using Bupivacain and Opioids
Versus Parenteral Opioids

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Background: Different types of analgesia have been proposed for the prevention of postoperative respiratory complications. The aim of this prospective, double-blind randomized study was to compare the impact of epidural bupivacaine and opioids versus parenteral opioids on respiratory complications in patients who had undergone major abdominal surgery.

Methods: One hundred fifty-three patients undergoing abdominal surgery for cancer were randomly allocated to receive either general anesthesia with intravenous fentanyl and postoperative analgesia with subcutaneous morphine (SC group) or general anesthesia combined with epidural bupivacaine and epidural bupivacaine plus morphine for postoperative pain relief (EP group). Analgesia was tested on a visual analog pain scale. Pulmonary complications were evaluated according to clinical complications, chest radiographs, arterial blood gas analysis, and pulmonary function tests. The evaluation was carried out on the day before the operation and on the first 5 postoperative days. Particular attention was also paid to the episodes of arterial hypotension and hemoglobin oxygen desaturation during the 1st postoperative night.

Results: Pain relief was significantly better in the EP group than in the SC group (P < 0.05) especially during recovery and on the 1st and 2nd postoperative days. In the EP group, vital capacity decreased less on the 1st postoperative day (P < 0.05) and arterial oxygen tension was greater in the recovery room (P < 0.05). However, no statistically significant difference was observed between the SC and EP groups in the incidence of clinical pulmonary complications (31% and 27%, respectively) and radiographic chest abnormalities (52% and 46%, respectively). The EP group recovered intestinal function earlier (P < 0.05), but significantly more patients in this group had episodes of systolic hypotension (21% vs. 8%; P < 0.05) during the 1st postoperative night. The length of the hospital stay was similar in both groups of treatment.

Conclusions: Epidural analgesia with a combination of local anesthetic and opioid improves patient comfort. However, this type of analgesia does not decrease the incidence of postoperative pulmonary complications, does not reduce the length of the hospital stay, and carries the risk of complications from episodic systemic hypotension. (Key words: Anesthetic techniques: epidural. Complications: postoperative morbidity; pulmonary complications. Pain: postoperative. Surgery: abdominal.)

SOME studies have suggested that epidural analgesia per se may improve postoperative respiratory mechanics when compared with parenteral opioid analgesia.1-3 However, these results have not been confirmed by other investigators.4,5 Diaphragmatic dysfunction, a major cause of respiratory complications after upper abdominal surgery, is not modified by the administration of opioids in the epidural space.6 Using clinical, radiologic, spirometric, and oxygenation criteria, we reported a similar incidence of pulmonary complications in a prospective study of 150 patients who received either parenteral or epidural morphine after abdominal surgery for cancer.5

In contrast, the administration of epidural local anesthetics and opioids may improve postoperative diaphragmatic function and gas exchange.7,8 Although some studies have reported fewer pulmonary complications with epidural bupivacaine compared to parenteral morphine,9,10 others did find no difference in postoperative respiratory complications using these two analgesic regimens.11-13 This discrepancy may be due to one of the following: 1) the studies were not
always carried out on a large, homogeneous group of patients undergoing the same type of surgery; 2) the definitions of pulmonary complications were different and not always included before the study; 3) the complication rate depended on the criteria that were used; or 4) the level of analgesia may have been insufficient to counteract the mechanisms underlying the development of pulmonary complications.

The benefits of epidural analgesia during and after anesthesia must be balanced against possible adverse effects. Dose-related respiratory depression can occur with epidural morphone or with parenteral morphone. Epidural analgesia with local anesthetics may be associated with a bilateral sympathetic and motor blockade, resulting in hypotension and paralysis in a small percentage of patients.

Therefore, we carried out a prospective, double-blind randomized study to compare the rate of postoperative clinical pulmonary complications, abnormalities on chest radiographs, and the duration of the hospital stay after major abdominal surgery for cancer between two large groups of patients. The first group (SC group) received general anesthesia followed by a continuous subcutaneous infusion of morphine, and the second group (EP group) received a combination of epidural and general anesthesia followed by continuous epidural infusion of bupivacaine and morphine. Comparisons also were made with respect to changes in arterial oxygenation and pulmonary function, and particular attention was paid to any episodes of systemic hypotension, motor blockade, and infectious complications resulting from the use of epidural catheters.

Materials and Methods

Patient Selection and Protocol

This prospective study was carried out for 14 months after approval was obtained from the local institutional ethical committee. Informed consent was obtained from each patient. Inclusion criteria were: 1) elective major abdominal surgery for cancer via midline or bilateral incision, 2) absence of contraindications to epidural anesthesia (e.g., preoperative coagulopathy, localized infection), and 3) absence of extreme malnutrition or cerebral vascular insufficiency.

Preoperative respiratory status was assessed by clinical examination, chest radiography, and arterial blood gas analysis. Vital capacity (VC) and forced expiratory volume in 1 s (FEV₁) were measured using a dry spirometer (Vitalograph Medical instrumentation, Buckingham) on the day before surgery. A history of respiratory disease is one of the main factors predisposing to postoperative pulmonary complications. To avoid an imbalance between the number of patients with a previous history of respiratory disease in the two treatment groups, the randomization was stratified for this factor. Patients were divided into two strata: those without a history of bronchopulmonary disease (non-BPD) and those with prior bronchopulmonary disease (BPD). Inclusion criteria in the BPD stratum were a chronic productive cough for more than 2 yr and/or one spirometric value below 60% of the normal value. Patients, in each stratum, then were randomized to receive either epidural or subcutaneous analgesia.

All the patients were premedicated with 2.5 mg lorazepam by mouth. In both groups, general anesthesia was induced with 0.3 mg/kg etomidate and 1.5 µg/kg intravenous fentanyl, and tracheal intubation was facilitated by 0.08 mg/kg vecuronium. All patients’ lungs were mechanically ventilated with a mixture of oxygen and nitrous oxide (fraction of inspired oxygen = 0.3) using a partially rebreathing circle system with a fresh gas flow rate of 3 L/min. Anesthesia was maintained with 1–2% isoflurane and muscle relaxation was provided by a further injection of vecuronium using train-of-four monitoring. All patients’ lungs were ventilated when they left the operating room. The total isoflurane used was measured by weighing the contents of the vaporizer before and after anesthesia. Patients were warmed to 36°C before tracheal extubation, and relaxants were antagonized when train-of-four stimulation produced four responses. After extubation, oxygen was administered through a nasal cannula when the hemoglobin oxygen saturation was less than 90%.

In the SC group, analgesia was provided by 7 µg/kg fentanyl before the skin incision. Reinjections of 2 µg/kg fentanyl were repeated as required. At the end of the surgical procedure, an epidural catheter was inserted into the subcutaneous tissue in such a way that it could not be distinguished from an epidural catheter positioned in the epidural space. Upon arrival in the recovery room, continuous morphine infusion (2.5 mg/h) was started through this catheter.

In the EP group, an epidural catheter was introduced at the T7–T11 level before surgery. A subcutaneous 5-cm tunneling of the epidural catheter was performed to provide additional prevention from infection. Bupivacaine 0.25% (20 ml) with epinephrine (1: 200,000) was injected. Bupivacaine was reinjected.
until the block attained the T4 level. When this level was obtained, general anesthesia was induced by the same anesthetic procedure used for the SC group. Intraoperative analgesia was obtained by intermittent epidural injections of 0.25% bupivacaine. Fentanyl was administered intravenously when bupivacaine failed to provide sufficient pain relief during surgery. Postoperatively, a mixture with bupivacaine 0.125% (10 ml/h) and morphine (0.25 mg/h) was infused continuously into the epidural space. Paracetamol (2 g/4 h) was injected intravenously on request in both groups when pain relief was inadequate. The analgesic treatment was continued at the same doses until the 5th day.

The postoperative bupivacaine-and-morphine or morphine-only solution syringes were filled and labeled by the hospital pharmacy. The nurses in charge of the patients were blinded to the contents of the syringes.

All patients received the same postoperative physiotherapy using incentive spirometry twice a day, irrespective of their history of respiratory disease. Physiotherapists were unaware of the type of analgesia used. The day after surgery (D1), the patients routinely sat in their armchair with the help of the nurse.

Postoperative Pain Assessment

To quantify the severity of postoperative pain, the patients were asked to use a 10-cm visual analog scale graded from 0 (no pain) to 10 (the most severe pain imaginable). Each morning of the first 5 postoperative days, all patients scored their pain at rest and while coughing. Furthermore, the number of days that elapsed before the first passage of gas after the end of surgery was recorded from the patient report.

Pulmonary Complications

A clinical examination was carried out on the day before surgery and each morning of the first 5 postoperative days for each patient. Clinical pulmonary complications were graded as described previously: cough, 1; purulent sputum, 2; rhonchi, 3; localized consolidation at physical examination, 2; fever, 1. A score greater than or equal to 3 on 2 consecutive days was defined as a clinical complication.

Chest radiographs were obtained preoperatively and on days 1, 3, and 5 after surgery. These films were interpreted at the end of the study by the same radiologist blinded to the patient's treatment and clinical status. To assess the reproducibility of the radiologic interpretation, all chest radiographs of 30 patients chosen by randomization were interpreted a second time by the same radiologist. Radiographic chest abnormalities were divided into three groups: lamellar atelectasis or small infiltrates, segmental atelectasis or large infiltrates, and pleural effusion.

Assessment of Lung Function

Blood gas analysis was carried out on days 1, 3, and 5 with patients breathing ambient air. Pulmonary function tests were performed by the anesthesiologist investigators who were trained to conduct these investigations before the study began. Vital capacity and FEV1 were measured daily using a dry spirometer with the patient in the sitting position. The best of three efforts was used to compare a prediction based on age, height and sex.

During the 1st postoperative night, arterial hemoglobin oxygen saturation (SPO2) was measured using a pulse oximeter (Oxytrak, Critikon, Tampa, FL) with an adhesive-backed probe; data were recorded every 5 min. An SPO2 of less than 85% on two consecutive measurements was the definition chosen for significant severe desaturation. Probe contact (saturation and plethysmography) was checked routinely and systematically when SPO2 was less than 90%.

Hemodynamic Assessment and Motor Blockade

Arterial blood pressure and heart rate were recorded every 5 min intraoperatively and during recovery. Maximal and minimal values were compared between the two groups. When systolic arterial blood pressure decreased to less than 80 mmHg, ephedrine was injected in 3-mg increments. These parameters also were recorded postoperatively every 10 min for 20 h (Oxytrak, Critikon).

The number of episodes of low systolic blood pressure (<80 mmHg) and elevated systolic blood pressure (>180 mmHg) were compared during this period between the two groups.

Motor function of the lower limbs was assessed daily by the patient's ability to flex the knees and ankles. The motor blockade was evaluated in terms of a modified four-grade Bromage scale:16

0 = No paralysis.
1 = Inability to raise extended leg (just able to move knee and feet).
2 = Inability to flex knee (able to move feet or first digit only).
3 = Inability to move any joint in the legs.
Bacteriologic Assessment
All epidural and subcutaneous catheters were withdrawn on the 5th postoperative day, and a quantitative culture of the catheter tip was obtained. The microorganisms and the number of colony-forming units/milliliter (CFU/ml) were identified as described before. Only catheter tips growing more than $10^3$ CFU/ml were taken into account.

Statistical Analysis
In our previous study, a 50% incidence of abnormalities was observed on the chest radiographs. On the basis of this data, we estimated that 150 patients would be required to demonstrate a difference of 25% between radiologic complication rates with a 5% type I error and a 10% type II error using a two-tail test. The data were collected on specific forms and entered into a Vax 11/785 computer (Digital, Maynard, MA). Consistency checks and descriptive statistical analysis were performed using the PIGAS database management system.

Preoperative patient characteristics in the two randomized groups were compared using chi-square analysis for category variables and the Student's $t$ test for continuous variables.

Postoperative assessment for all variables measured over time were evaluated using repeated measures analysis of variance techniques using Statistical Analysis System (SAS, Cary, NC).

Postoperative category variables were compared by chi-square analysis. When preoperative patient characteristic variables were significantly correlated with outcome variables, stratified chi-square tests were performed and analysis of variance was done by taking into account the main effects and interaction terms when necessary. To assess the reproducibility of the radiologic interpretation, the Kappa coefficient was computed and tested by the usual method.

Results

Patient Characteristics
One hundred sixty-three patients were assigned randomly to one of the two analgesia groups. Ten patients were excluded for the following reasons: early surgical complications ($n = 4$), postoperative ventilator dependence ($n = 1$), associated thoracotomy ($n = 1$), intraoperative anaphylaxis ($n = 1$), and surgery cancelled after randomization ($n = 3$). Four of these patients were in the EP group. Therefore, 153 patients were considered eligible for further study.

These patients represented 68% of the total number who underwent major abdominal surgery in our institution during the 14 months of the study. The two groups of patients were similar with respect to weight, age, and history of respiratory disease. However, significantly more smokers and more males were in the SC group (table 1). Since both of these variables were correlated (30% smokers among men, 7% among women; $P < 0.01$), analyses were stratified according to smoking status. During surgery, no differences were observed in intravenous fluid requirements, in the amounts of etomidate or vecuronium, or in the duration of anesthesia (table 2).

Patients in the EP group received less isoflurane and fentanyl than did patients in the SC group; only one patient in the EP group received more than 1.5 $\mu$g/kg intravenous fentanyl (table 2). The administration of ephedrine was significantly more frequent in the EP group ($15 \pm 10$ mg in 52 patients) than in the SC group ($9 \pm 5$ mg in 4 patients). At the end of surgery, central body temperature was significantly lower in the EP group than in the SC group, and it was similar in both groups at the departure from recovery room (table 2). The duration of postoperative mechanical ventilation was similar in both groups (table 2).

Table 1. Comparison of the Two Treatment Groups for Preoperative Factors

<table>
<thead>
<tr>
<th></th>
<th>EP Group</th>
<th>SC Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients</td>
<td>78</td>
<td>75</td>
</tr>
<tr>
<td>Age (yr)</td>
<td>56 ± 11</td>
<td>56 ± 14</td>
</tr>
<tr>
<td>Sex</td>
<td>43M/35F</td>
<td>55M/20F</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>72 ± 14</td>
<td>71 ± 13</td>
</tr>
<tr>
<td>History of smoking</td>
<td>n = 11</td>
<td>n = 22*</td>
</tr>
<tr>
<td>(14%)</td>
<td>(29%)</td>
<td></td>
</tr>
<tr>
<td>Respiratory disease</td>
<td>n = 16</td>
<td>n = 14</td>
</tr>
<tr>
<td>(21%)</td>
<td>(19%)</td>
<td></td>
</tr>
</tbody>
</table>

Values are mean ± SD. EP = epidural analgesia; SC = Intravenous and subcutaneous analgesia.

* $P < 0.05$, between the two groups.
Table 2. Comparison of the Two Treatment Groups during Anesthesia

<table>
<thead>
<tr>
<th></th>
<th>EP Group</th>
<th>SC Group</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean duration of anesthesia (min)</td>
<td>225 ± 90</td>
<td>215 ± 81</td>
</tr>
<tr>
<td>Fentanyl iv (µg)</td>
<td>119 ± 88</td>
<td>757 ± 294*</td>
</tr>
<tr>
<td>Bupivacaine (mg)</td>
<td>70 ± 25</td>
<td>0</td>
</tr>
<tr>
<td>Etomidate (mg)</td>
<td>21 ± 3.3</td>
<td>21 ± 3.6</td>
</tr>
<tr>
<td>Isoflurane (mg)</td>
<td>55 ± 31</td>
<td>73 ± 38*</td>
</tr>
<tr>
<td>No. of patients having</td>
<td></td>
<td></td>
</tr>
<tr>
<td>received ephedrine</td>
<td>n = 52</td>
<td>n = 4*</td>
</tr>
<tr>
<td>Vecuronium (mg)</td>
<td>17 ± 6</td>
<td>16 ± 5</td>
</tr>
<tr>
<td>Crystalloids (ml)</td>
<td>2806 ± 974</td>
<td>2699 ± 906</td>
</tr>
<tr>
<td>Albumin 4% (ml)</td>
<td>866 ± 465</td>
<td>963 ± 445</td>
</tr>
<tr>
<td>Blood transfusion (ml)</td>
<td>1119 ± 637</td>
<td>1125 ± 750</td>
</tr>
<tr>
<td>Temperature at the end of surgery (*C)</td>
<td>34.9 ± 0.8</td>
<td>35.2 ± 0.8*</td>
</tr>
<tr>
<td>Temperature before leaving recovery room (*C)</td>
<td>37.1 ± 0.8</td>
<td>37.4 ± 0.9</td>
</tr>
<tr>
<td>Duration of postoperative mechanical ventilation (min)</td>
<td>61 ± 43</td>
<td>71 ± 42</td>
</tr>
</tbody>
</table>

Values are mean ± SD. EP = epidural analgesia; SC = intravenous and subcutaneous analgesia.

*P < 0.05, between the two treatment groups.

Postoperative Analgesia

In the recovery room (D0), 1 patient in the EP group and 11 patients in the SC group were unable to score their pain on the visual analog scale. Epidural analgesia provided significantly better analgesia at rest or with a cough during the first 2 postoperative days (figs. 1 and 2). At D0, significantly more patients required intravenous administration of paracetamol in the SC group (52%) than in the EP group (17%; P < 0.05). The number of patients who were pain-free at rest was significantly greater in the EP group (D0 64%, D1 52%) than in the SC group (D0 22%, D1 29%). All of these differences persisted up to the 2nd day after recovery.

In the EP group, partial motor blockade occurred in seven patients (5 patients grade 1, 2 patients grade 2) on the 1st postoperative day, in three patients (2 patients grade 1, 1 patient grade 2) on the 2nd postoperative day, and in two patients (grade 1) each on the 3rd and 4th postoperative days.

Pulmonary Complications

The two groups had similar clinical complication and radiologic abnormality rates (table 3). The second interpretation of abnormalities on chest radiographs of 30 patients was closely correlated with the

![Image](http://anesthesiology.pubs.asahq.org/pdfaccess.ashx?url=/data/journals/jasa/931320/)

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In the recovery room, the $P_{aO_2}$ was significantly higher in the EP group compared to that in the SC group (fig. 4). After D0, oxygenation was not statistically different between the two groups up to the 5th day as expressed by $P_{aO_2}$ (fig. 4). During the 1st night after surgery, 30 patients in the EP group and 33 patients in the SC group had at least one episode of $S_{pO_2}$ between 85% and 90%. Five patients in the EP group presented at least one episode of $S_{pO_2}$ less than 85%, compared to 10 patients in the SC group.

Thirty patients (20%) were included in the BPD stratum (table 4), and 30% of them had a history of chronic bronchitis. A statistical difference was observed in VC, $FEV_1$, and $P_{aO_2}$ ($P < 0.05$) between patients in BPD and non-BPD strata (table 4). Of the 30 patients, 7 had a normal VC (75–100% of the predicted value), 10 had a moderate reduction (65–75% of the predicted value), and 13 had a severe reduction (45–65% of the predicted value). The $FEV_1$ was normal in 7 patients, moderately reduced in 4, and severely reduced in 19. Eight patients had a $FEV_1/VC$ ratio below 65%, and four

Table 4. Preoperative Spirometry and Postoperative Respiratory Complications in the Two Treatment Groups, According to the History of Respiratory Disease

<table>
<thead>
<tr>
<th></th>
<th>Non-BPD Patients</th>
<th>BPD Patients</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 123)</td>
<td>(n = 30)</td>
</tr>
<tr>
<td>Preoperative spirometry</td>
<td></td>
<td></td>
</tr>
<tr>
<td>VC (% of predicted value)</td>
<td>$91 \pm 16$</td>
<td>$69 \pm 17^*$</td>
</tr>
<tr>
<td>$FEV_1$ (% of predicted value)</td>
<td>$88 \pm 16$</td>
<td>$58 \pm 17^*$</td>
</tr>
<tr>
<td>$P_{aO_2}$ (mmHg)</td>
<td>$89 \pm 13$</td>
<td>$81 \pm 12^*$</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mmHg)</td>
<td>$38 \pm 4$</td>
<td>$39 \pm 4$</td>
</tr>
<tr>
<td></td>
<td>EP Group (n = 62)</td>
<td>SC Group (n = 61)</td>
</tr>
<tr>
<td></td>
<td>EP Group (n = 18)</td>
<td>SC Group (n = 14)</td>
</tr>
<tr>
<td>Respiratory complications</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Clinical complications</td>
<td>$14$ (23%)</td>
<td>$7$ (44%)</td>
</tr>
<tr>
<td>Chest radiograph abnormalities</td>
<td>$25$ (42%)</td>
<td>$10$ (63%)</td>
</tr>
<tr>
<td>$P_{aO_2}$ (mmHg) in recovery room</td>
<td>$83 \pm 14$</td>
<td>$69 \pm 11$</td>
</tr>
<tr>
<td>$P_{aCO_2}$ (mmHg) in recovery room</td>
<td>$40 \pm 4$</td>
<td>$39 \pm 5$</td>
</tr>
</tbody>
</table>

BPD or non-BPD patients = patients with or without history of bronchopulmonary disease; EP = epidural analgesia; SC = intravenous and subcutaneous analgesia; VC = vital capacity; $FEV_1$ = forced expiratory volume in 1 s; $P_{aO_2}$ and $P_{aCO_2}$ = oxygen and carbon dioxide arterial tension.

* $P < 0.05$, between the two strata.
† $P < 0.05$, between the two treatment groups.
of these eight patients had a normal VC. In BPD patients, 
$P_{aO_2}$ values varied from 66 to 100 mmHg. Eleven pa-

tients had values between 70 and 79 mmHg, and 5 
between 65–69 mmHg. Less variability was noted for 
$P_{aCO_2}$ values (32–48 mmHg); $P_{aCO_2}$ was 45 mmHg or 
higher in three patients and between 42 and 45 mmHg 
in two patients. The difference in the incidence of clin-
ic complications and radiologic abnormalities was 
not statistically significant between the two treatment 
groups (table 4).

A statistically significant difference between the two 
treatment groups for postoperative $P_{aO_2}$ was observed 
only for non-BPD patients in the recovery room (ta-

ble 4).

**Adverse Effects**

The maximal systolic arterial pressure was similar 
during surgery but was significantly greater during re-
covery and during the 1st night in the SC group com-
pared to that in the EP group (fig. 5). The minimum 
systolic arterial pressure was higher in the SC group 
compared to that in the EP group during and after sur-
gery. During the 1st postoperative night, the number 
of episodes of high blood pressure was similar in both 
groups, but the incidence of systolic hypotension (<80 

mmHg) was significantly greater in the EP group than 
in the SC group (21% and 8%, respectively; $P < 0.05$).

Minimal or maximal heart rates were not different 
between the two groups except during recovery, when 
the maximal heart rate was greater in the SC group 
($112 \pm 24$ vs. $101 \pm 18$; $P < 0.01$).

Bacteriologic results were available for 70 of the 78 
epidural catheters. A positive culture ($>10^3$ CFU/ml) 
was found in four catheters (6%), three with *staphy-
lococcus epidermidis* and one with *staphylococcus aureus*. A subcutaneous abscess with *s. aureus* developed 
in one patient. None of these patients developed neurologic complications.

The recovery of intestinal gas transit was earlier in 
the EP group than in the SC group ($P < 0.05$; fig. 6).

The length of the hospital stay was $18 \pm 7$ days in 
the EP group and $16 \pm 6$ days in the SC group, which is 
not significantly different.

**Discussion**

The combination of an extradural local anesthetic 
and an opioid resulted in good pain relief, less of a 
decrase in the $P_{aO_2}$ in the recovery room, and an im-
provement in the VC on the 1st postoperative day, but
no significant effect was observed on late postoperative respiratory complications (table 3). No difference was found between the two treatment groups regardless of the patient’s history of smoking or the criteria chosen for respiratory complications. The potential shortcoming in our classification of clinical pulmonary complications is the subjectivity of the physical examination. However, in our previous study, the physical examination was carried out by the same three independent investigators (two physicians and one physiotherapist), and the scores were closely correlated (P < 10⁻⁴) by the Kappa coefficient of agreement. Even though we conducted a randomized study, the sex ratio and the number of smokers were unbalanced between the two treatment groups. Therefore, we did a statistical adjustment for these two parameters. These adjustments did not allow the difference between the two groups to become statistically significant. Smoking is a known risk factor for postoperative pulmonary complications. As significantly more smokers were in the SC group, a predominance of pulmonary complications might have been expected among these patients. Contrary to expectations, this was not the case, and moreover, the greater number of smokers in the SC groups adds further weight to the conclusion that epidural analgesia does not decrease respiratory complications. Furthermore, the statistical adjustment did not alter the significant differences in the results probably because the randomization of these patients was stratified on the history of previous respiratory disease (see Patient Selection and Protocol), and the number of smokers with an altered respiratory status was balanced between the two groups.

The increased PaO₂ in the recovery room in the EP group compared to that of the SC group could be attributed either to the beneficial effect of epidural analgesia on postoperative pulmonary function 1,8 or to the use of a low dose of fentanyl during anesthesia, which reduces postoperative respiratory depression. Despite this difference, no difference was found in the duration of postoperative mechanical ventilation. The duration of postoperative mechanical ventilation can be influenced by nonrespiratory factors, including body temperature (table 2).

Episodic arterial hemoglobin desaturation may occur during the 5 postoperative days 20 especially when parenteral morphine is given. 15 For technical reasons, SpO₂ was continuously measured only during the 1st postoperative night. The number of patients with nasal oxygen and with episodic arterial hemoglobin desaturation was slightly lower in the EP group than in the SC group. Nevertheless, interpretation is impeded by variable effects of oxygen therapy on the correction of the episodic arterial hemoglobin desaturation. 20,21 The fraction of inspired oxygen was undefined because a nasal cannula was used for the delivery of oxygen and this would have affected the quality of the comparison. Therefore, we did not carry out statistical analysis on this comparison.

This study indicates that epidural analgesia after major surgery does not lead to a decrease in respiratory morbidity. In a pathophysiologic study, Mankikian et al. 7 found that an epidural block with 0.5% bupivacaine (between 8 and 14 ml) on the 1st postoperative day was associated with a partial improvement of diaphragmatic dysfunction and forced vital capacity. However, functional residual capacity and arterial blood gases remained unchanged after epidural injection. Other authors used continuous infusion of bupivacaine over a longer period (24–48 h) and found an improvement in postoperative pulmonary function tests compared to the use of parenteral analgesia. 9,22 However, epidural analgesia does not afford a dramatic benefit for postoperative respiratory morbidity according to certain authors. 11–15 It is difficult to give systematic explanations for this discrepancy, since the definitions of pulmonary complications, the numbers of patients studied, and the types of surgery often differ.

We concentrated our efforts on providing optimal postoperative pain relief using a combination of agents because of ample evidence that pain relief cannot be achieved by a single agent or method without significant side effects, unless there is major investment in equipment and surveillance systems. 14,15,25 Continuous epidural infusions of different opioids plus local anesthetic are the standard of treatment in other institutions. 9,23–26 In this study, continuous infusion of an extradural local anesthetic (0.125% bupivacaine, 10 ml/h) combined with morphine (0.25 mg/h), provided satisfactory pain relief after major intraabdominal surgery for cancer. Nevertheless, analgesia was not complete for every patient. The percentage of postoperative pain-free patients (1st day 52%) in this study is similar to the 60% 27 and 59% 12 rates reported in prior studies using epidural analgesia. The suboptimal pain relief may be explained by low doses of the analgesic (concentration or flow rate), 28 tachyphylaxis, 29,30 catheter misplacement, or a change in the pharmacokinetics of
the local anesthetic during the postoperative period. An increase in either the concentration or the flow rate of bupivacaine can induce severe adverse effects and lead to potentially toxic plasma concentration. With 0.125% bupivacaine (20 ml/h) over a 44-h delivery period, high plasma concentrations of bupivacaine were found, but no obvious signs of toxicity were observed. An increased dose of morphine, either in the epidural space or via the parenteral route, would have provided better analgesia but a higher risk of severe adverse effects. The dose of epidural morphine used in this study has been reported to be safe. The contribution of phrenic nerve afferents and the visceral components of nociceptive afferents may explain, in part, the insufficiency of analgesia in some patients. Finally, tachyphylaxis could be the reason why the superiority of epidural analgesia lasted for only 2 days despite the low bupivacaine concentration used. Under the conditions of this study, epidural analgesia did not offer an advantage over parenteral analgesia after 48 h.

Because of the small number of BPD patients in this study, no definitive conclusion can be drawn regarding an advantage of epidural analgesia for the prevention of postoperative respiratory complications in this group. Studies performed on a large number of patients would reduce the risk of a type II error. Two controlled studies have found a reduction in the overall postoperative complication rate (including cardiovascular, respiratory, renal failure, and others) in a population of high-risk surgical patients given epidural anesthesia and postoperative epidural analgesia compared to that of a group of patients given general anesthesia and postoperative parenteral analgesia. Yeager et al. also found a reduction in postoperative mortality in the group that received epidural analgesia. However, these investigators did not find a statistically significant difference between the two groups in respiratory failure. Baron et al. found no difference in postoperative morbidity, including respiratory complications, between epidural and general anesthesia for vascular surgery in high-risk patients. To our knowledge, postoperative pain relief by extradural opioid and/or local anesthetics has not clearly demonstrated that it was able to reduce postoperative respiratory morbidity after major abdominal procedures.

Epidural catheter contamination rates have been reported to range from 0 to 28% for a duration of 3 h to 6 days in different types of surgery. Clinically significant infectious complications from epidural anesthesia are rare. We did not observe any neurologic complications. One patient experienced a subcutaneous abscess that required drainage and treatment with antibiotics.

Epidural analgesia with local anesthetics can cause systemic hypotension and even paralysis of the lower extremities. In our study, the patients in the EP group were significantly more hypotensive during surgery and the 24-h postoperative period. The incidence of systemic hypotension in our study (21%) is similar to others, varying from 25% to 23% and 14%. Although systemic hypotension responded readily to treatment, and because sympathetic blockade depends on the level of epidural analgesia, it limits the use of higher doses of bupivacaine and is an indication for prolonged monitoring of systemic blood pressure during the postoperative period. The use of higher doses of epidural morphine leads to more potential side effects, particularly respiratory depression; thus, patients must be monitored closely. However, in a study in which 1,106 patients received epidural morphine postoperatively on regular surgical wards, Ready reported a 0.2% incidence of respiratory depression. These two cases of major side effects occurred with a low dose of epidural morphine and were reversed by intravenous naloxone. The authors concluded that epidural morphine can be used effectively and safely to provide postoperative analgesia on surgical wards.

Epidural anesthesia with local anesthetics does not influence gastric emptying and exerts less of an effect than that with parenteral opioids on clinical subjects. In our study, as in others, we found that a reduction in the use of opioids helps to avoid their depressant effects on gastrointestinal function.

Finally, there was no difference between the two groups for the length of the hospital stay. The hospital stay, including time to ambulation, can be considered a means of measuring overall postoperative morbidity. Several controlled studies measured the length of stay following either epidural analgesia or parenteral analgesia and found no difference except for two studies. In one, continuous epidural analgesia was found to shorten the hospital stay after hip surgery but not after upper abdominal surgery. In the other study, the patients were grossly obese and not comparable with a general population of surgical patients.

In summary, our prospective randomized study of 153 patients demonstrated that postoperative epidural
analgesia with a local anesthetic and an opioid provides good pain relief but does not reduce either postoperative respiratory morbidity or the length of hospital stay. After 48 h, epidural analgesia is equivalent to parenteral analgesia. Epidural postoperative analgesia may become a standard form of treatment for patients undergoing major abdominal surgery, but each case should be considered individually with regard to benefits versus risks.

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