

Efficacy of Postoperative Patient-controlled and Continuous Infusion Epidural Analgesia versus Intravenous Patient-controlled Analgesia with Opioids

A Meta-analysis

Christopher L. Wu, M.D.,* Seth R. Cohen, B.S.,† Jeffrey M. Richman, M.D.,‡ Andrew J. Rowlingson, B.A.,§ Genevieve E. Courpas, B.A.,§ Kristin Cheung, M.D.,|| Elaina E. Lin, B.A.,# Spencer S. Liu, M.D.**

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The authors performed a meta-analysis and found that epidural analgesia overall provided superior postoperative analgesia compared with intravenous patient-controlled analgesia. For all types of surgery and pain assessments, all forms of epidural analgesia (both continuous epidural infusion and patient-controlled epidural analgesia) provided significantly superior postoperative analgesia compared with intravenous patient-controlled analgesia, with the exception of hydrophilic opioid-only epidural regimens. Continuous epidural infusion provided statistically significantly superior analgesia *versus* patient-controlled epidural analgesia for overall pain, pain at rest, and pain with activity; however, patients receiving continuous epidural infusion had a significantly higher incidence of nausea–vomiting and motor block but lower incidence of pruritus. In summary, almost without exception, epidural analgesia, regardless of analgesic agent, epidural regimen, and type and time of pain assessment, provided superior postoperative analgesia compared to intravenous patient-controlled analgesia.

DESPITE the availability of postoperative pain guidelines,¹ postoperative pain continues to be undertreated^{2,3} and may result in a variety of unfavorable short- and long-term outcomes.^{4–6} Of the two major analgesic options (epidural analgesia *vs.* systemic opioids) after inpatient surgery, the overall benefits of postoperative epidural analgesia on mortality and major morbidity are controversial with available larger observational, randomized controlled trials and meta-analyses equivocal for the efficacy of epidural analgesia in improving perioperative outcomes.^{7–14} However, systematic analysis of available nonrandomized and randomized trials^{15,16} seem to indicate that postoperative epidural an-

algesia will provide superior analgesia when compared with that from systemic opioids.

Even though epidural analgesia seems to provide better postoperative pain control than systemic opioids, this comparison in some sense may not be meaningful because categorizing systemic opioids (which includes intramuscular, subcutaneous, intravenous, and intravenous patient-controlled analgesia [PCA]) into a single generic entity may not reflect the actual clinical use of postoperative opioids, which may be primarily delivered *via* intravenous PCA.^{1,17,18} To truly determine the analgesic value of epidural analgesia for postoperative pain management, it would be appropriate to compare patient-controlled epidural analgesia (PCEA) with intravenous PCA, which many believe is the accepted standard for delivery of opioid analgesia postoperatively. We performed a meta-analysis of the analgesic efficacy of postoperative PCEA and continuous epidural infusion (CEI) analgesia to intravenous PCA with opioid. To minimize duplication of data and results from our previous publication,¹⁵ we used a different literature search strategy and attempted to acquire additional unpublished data from studies that had not been available for our previous meta-analysis.

Materials and Methods

The National Library of Medicine's PubMed database was searched for the time period 1966 to August 4, 2004. PubMed was searched for all articles containing text words *PCA* or *patient-controlled analgesia* (9,122 articles), which was combined with the text word *epidural* (25,480 articles) using the usual Boolean meanings of *AND*. The result was 757 articles. This search was limited to the English language (650 articles) and then the Randomized Controlled Trials function, which resulted in 299 abstracts. The full article of each of the 299 abstracts was then reviewed by one of the authors for inclusion into the meta-analysis. No minimum sample sizes were invoked for inclusion of studies in the analysis. Any disputes were resolved by agreement of at least two reviewers. After selecting the initial articles, the authors' personal files were checked for any additional studies.

For the purposes of this meta-analysis, postoperative

* Associate Professor, ‡ Assistant Professor, § Research Associate, || Senior Instructor, # Medical Student, Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins University, Baltimore, Maryland. † Medical Student, Philadelphia College of Osteopathic Medicine, Philadelphia, Pennsylvania. ** Clinical Professor, Department of Anesthesiology, Virginia Mason Medical Center, University of Washington, Seattle, Washington.

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Address reprint requests to Dr. Wu: Johns Hopkins University, Carnegie 280, 600 North Wolfe Street, Baltimore, Maryland 21287. Address electronic mail to: chwu@jhmi.edu.

epidural analgesia was defined as a primarily local anesthetic or opioid-based analgesic regimen delivered into the epidural space by CEI or PCEA over at least a 24-h period after a surgical procedure. Patient-controlled analgesia was defined as delivery of analgesic medication either through the epidural or intravenous catheter *via* a mechanical PCA device. Only studies that compared postoperative epidural *versus* intravenous PCA with opioids using visual analog scale (VAS) measurements of pain or a similar substitute (e.g., numerical rating scale) in a randomized fashion were included. Only studies including primarily only adult patients (aged ≥ 18 yr) were allowed. To be included in this meta-analysis, studies had to have a clear comparison between epidural analgesia to intravenous PCA without any crossover or concurrent use of the alternate regimen (e.g., concurrent use of intravenous PCA during a dose-finding study of postoperative epidural analgesia, which might include a normal saline epidural control group). Exclusion criteria included articles where VAS pain scores could not be recorded or extrapolated from the data provided in the article. Studies of epidural analgesia that only gave a single epidural dose at the time of surgery (single shot) or by repeated healthcare provider epidural bolus dosing were not included.

Data (e.g., VAS pain scores, number of subjects, type of epidural regimen, study characteristics) were abstracted from each article, and the results were recorded. Data were extrapolated from figures as needed; however, an attempt was made to contact the original authors before extrapolation. Definition of complications was recorded as originally defined by the study. We then recorded the incidence of that complication as reported by the study. For nausea and vomiting, we recorded the higher number if both were reported. In some cases, we could not translate a study's data into an incidence rate. In those studies, we did not enter that data into the database; however, we did incorporate the remainder of that study's data as feasible. For incomplete or uninterpretable data, we made an attempt to contact the corresponding author of the study in question.

All reported data were included as unique observations and subgrouped as described below. VAS or numeric pain scores were converted to a 0–10 scale. VAS data were weighted by sample size and, if a given article measured pain at multiple time points, all measurements were included in the analysis. Therefore, the *n* reported is the total number of patient observations (*i.e.*, one study of 10 patients that measured pain at 3 different time points would contribute an *n* of 30 to the overall sample size). The global mean VAS (weighted for patient observations) and for each postoperative day up to 3 days after surgery between epidural analgesia and intravenous PCA were compared. The data for epidural analgesia were subdivided by type of delivery (CEI *vs.* PCEA), analgesic regimen, and location/type of surgery, with a

subsequent comparison of the epidural analgesia to intravenous PCA performed. All epidural infusions containing local anesthetic were considered equivalent, including those with and without opioid. Both rest and incident (activity) pain were included in the global analysis; however, rest and incident pain were also analyzed separately and again divided into subgroups depending on various epidural characteristics as described above. Finally, the presence of minor complications (*i.e.*, nausea or vomiting [whichever was more frequent], sedation, pruritus, urinary retention, and motor block/weakness) were recorded.

A fixed effect model was used. The level of significance for all tests was set at an α of 0.05. A Kolmogorov test showed that the data were not normally distributed; instead, both epidural and intravenous PCA opioid data were positively skewed. Analysis of variance was used to compare VAS pain scores between treatment groups. The Bonferroni correction was used for multiple comparisons of postoperative day VAS data. For complication data, comparisons were made between two groups at a time with the chi-square test. All statistical analyses were performed with SPSS 11.5.1 (SPSS Inc., Chicago, IL). After the data compilation was complete, we performed further analyses to assess the validity of our conclusions. We performed an analysis of the file drawer problem (*i.e.*, how many unpublished studies or subjects showing no difference between treatment regimens would be needed to be “discovered” in someone's file drawer to invalidate our results) as described by Rosenthal.¹⁹

Results

The search resulted in 299 abstracts of which a total of 48 articles met all inclusion criteria. An additional 2 references from previous systematic reviews and other sources were also included, for a total of 50 articles (appendix). There were a total of 1,625 patients randomly assigned to epidural analgesia and 1,583 patients to intravenous PCA. A total of 251 articles were rejected for the following reasons: 235 were not comparisons of postoperative epidural analgesia *versus* intravenous PCA as defined in the Materials and Methods, 2 were not randomized, 4 did not report usable VAS or numeric pain scores, and 10 included pediatric subjects. The characteristics of included studies are shown in table 1. Articles measured pain after a wide variety of operations and came from medical centers all over the world. Pain was measured after abdominal surgery in 19 studies (38%), with thoracic (*n* = 10, or 20%) and lower extremity (*n* = 7, or 14%) surgery being the next most common types of surgery studied. Only 4% of the epidural patients received local anesthetic alone, whereas 28% (*n* = 14) received opioids alone and 68% (*n* = 34) received local anesthetic and opioid, with the choice of epidural opioid

Table 1. Characteristics of Included Studies

Surgical site	
Abdominal	19 (38)
Thoracic	10 (20)
Lower extremity	7 (14)
Cesarean delivery	2 (4)
Pelvic	6 (12)
Other	2 (4)
Multiple	3 (6)
Unspecified	1 (2)
Sex	
Women	7 (14)
Men	2 (4)
Both	39 (78)
Unspecified	2 (4)
Epidural site	
Lumbar	17 (34)
Thoracic	26 (52)
Mixed	2 (4)
Unspecified	5 (10)
Study location	
Europe	24 (48)
United States	14 (28)
Canada	7 (14)
Australia	3 (6)
Asia	2 (4)
Epidural type	
Continuous	34 (68)
PCEA	16 (32)
Epidural infusion	
Opioid alone	14 (28)
Local anesthetic + opioid	34 (68)
Local anesthetic alone	2 (4)
Epidural opioid	
Morphine	12 (24)
Fentanyl	19 (38)
Sufentanil	8 (16)
Hydromorphone	2 (4)
Mixed	1 (2)
Unspecified	6 (12)
None	2 (4)
Epidural local anesthetic	
Bupivacaine	24 (48)
Ropivacaine	9 (18)
Lidocaine	1 (2)
Unspecified	1 (2)
Other	1 (2)
None	14 (28)
Intravenous PCA with opioid	
Morphine	38 (76)
Fentanyl	3 (6)
Sufentanil	2 (4)
Hydromorphone	2 (4)
Meperidine	1 (2)
Other	4 (8)

Data are presented as number (%).

PCA = patient-controlled analgesia; PCEA = patient-controlled epidural analgesia.

being predominantly fentanyl (38%), followed by morphine (24%) and sufentanil (16%). The most commonly used epidural local anesthetic was bupivacaine (48%), followed by ropivacaine (18%). For intravenous PCA, morphine (76%) was most commonly used, followed by fentanyl (6%).

When all studies and observations were combined

(table 2), epidural analgesia overall provided superior postoperative analgesia compared with intravenous PCA with opioids ($P < 0.001$). Epidural analgesia provided significantly superior analgesia overall, for pain at rest, and for pain with activity ($P < 0.001$). The quality of analgesia may be different at different points in the postoperative recovery period, so pain scores were also assessed at different postoperative times. Epidural analgesia overall was superior to intravenous PCA opioid analgesia at all time points ($P < 0.001$ for each day up to 3 days after surgery) even when analyzed separately by pain at rest or pain with activity (table 2).

Table 3 shows the VAS pain scores for CEI ($n = 1,272$ subjects) *versus* PCEA ($n = 353$ subjects) *versus* intravenous PCA ($n = 1,583$ subjects). For all epidural (CEI or PCEA) comparisons *versus* intravenous PCA overall and for pain at rest and with activity, epidural analgesia provided significantly superior analgesia *versus* intravenous PCA with opioids ($P < 0.001$). When CEI was compared with PCEA, CEI provided significantly superior analgesia ($P < 0.001$) *versus* PCEA for overall pain, pain at rest, and pain with activity (table 3).

When comparing the different types of epidural regimens (opioid alone [hydrophilic *vs.* lipophilic] *vs.* local anesthetic + opioid *vs.* local anesthetic alone), all epidural regimens provided significantly superior analgesia *versus* intravenous PCA for overall pain, pain at rest, and pain with activity (table 4), with the exception of hydrophilic opioid-only regimens, which were primarily delivered *via* a PCA device. Compared with local anesthetic alone or local anesthetic plus opioid, epidural hydrophilic opioid alone provided significantly inferior analgesia ($P < 0.001$), but epidural lipophilic opioid alone provided comparable VAS scores overall and for pain with activity. Epidural local anesthetic plus opioid provided statistically equivalent analgesia (*vs.* epidural local anesthetic alone) for overall pain and pain with activity but inferior analgesia for pain at rest as compared with local anesthetic alone (table 4).

Finally, epidural analgesia overall provided significantly superior analgesia ($P < 0.001$) compared with intravenous PCA with opioids for all regions of surgery examined (thoracic, pelvic, abdominal, cesarean delivery, lower extremity, and multiple locations) (table 5). Studies where location of surgery was defined as "other" or "not specified" ($n < 110$ weighted observations for each group) were not included in these analyses. Rates for complications are shown in table 6. Compared with intravenous PCA, the epidural group had a lower incidence of nausea-vomiting and sedation but a higher incidence of pruritus, urinary retention, and motor block. When comparing CEI with PCEA, CEI provided statistically significantly superior analgesia ($P < 0.001$) *versus* PCEA for overall pain, pain at rest, and pain with activity; however, patients receiving CEI had a significantly higher incidence of nausea-vomiting and motor

Table 2. Aggregate VAS Pain Data

Parameter	Epidural Analgesia (N = 1,625)	Intravenous PCA (N = 1,583)	P Value
Overall data			
All data	2.1 ± 1.3 (n = 7,744)	3.2 ± 1.6 (n = 7,666)	< 0.001
Pain at rest—all data	1.6 ± 1.0 (4,482)	2.5 ± 1.2 (4,507)	< 0.001
Pain with activity—all data	2.8 ± 1.3 (3,262)	4.1 ± 1.7 (3,159)	< 0.001
Postoperative day 0			
All data	2.2 ± 1.6 (n = 1,416)	4.1 ± 1.6 (n = 1,469)	< 0.001
Pain at rest	1.9 ± 1.5 (941)	3.6 ± 1.4 (964)	< 0.001
Pain with activity	2.9 ± 1.6 (475)	5.0 ± 1.6 (505)	< 0.001
Postoperative day 1			
All data	2.4 ± 1.3 (n = 2,625)	3.6 ± 1.5 (n = 2,612)	< 0.001
Pain at rest	1.6 ± 0.9 (1,510)	2.6 ± 0.9 (1,522)	< 0.001
Pain with activity	3.4 ± 1.0 (1,115)	4.9 ± 1.1 (1,090)	< 0.001
Postoperative day 2			
All data	2.3 ± 1.2 (n = 2,022)	3.0 ± 1.4 (n = 1,971)	< 0.001
Pain at rest	1.6 ± 0.9 (1,125)	2.1 ± 0.8 (1,121)	< 0.001
Pain with activity	3.2 ± 1.0 (897)	4.3 ± 1.0 (850)	< 0.001
Postoperative day 3			
All data	1.4 ± 0.9 (n = 1,628)	1.8 ± 1.2 (n = 1,581)	< 0.001
Pain at rest	1.2 ± 0.8 (874)	1.7 ± 1.1 (868)	< 0.001
Pain with activity	1.5 ± 1.0 (754)	2.0 ± 1.4 (693)	< 0.001

Data are visual analog scale (VAS; 0–10) pain scores presented as mean ± SD.

n = weighted number of observations for each parameter; N = actual number of patients per group; PCA = patient-controlled analgesia with opioid.

block but lower incidence of pruritus. Within the epidural group, the majority of the subjects with motor block received CEI. Finally, we calculated the number of file drawer subjects needed to invalidate our results to be 2,567 subjects.

Discussion

Although epidural analgesia has been shown to provide superior analgesia compared with systemic opioids in systematic reviews,^{15,16} the analgesic efficacy of PCEA or CEI compared with the accepted standard, intravenous PCA, has not been separately assessed. We per-

formed a meta-analysis of randomized controlled trials and found that when compared with intravenous PCA, PCEA and CEI overall provided significantly superior postoperative analgesia at all time intervals up to 3 days after surgery. Epidural analgesia in every combination, with the exception of hydrophilic opioid-alone regimens, provided superior postoperative analgesia compared with intravenous PCA with opioids. It also seemed that CEI provided superior analgesia compared with PCEA and that epidural local anesthetics with or without opioid provided superior analgesia *versus* epidural opioid alone.

Although our current study is similar to our previous

Table 3. PCEA VAS Pain Data

Parameter	CEI (N = 1272)	PCEA (N = 353)	Intravenous PCA (N = 1583)
All data	2.0 ± 1.2 (n = 5,908)	2.3 ± 1.4 (n = 1,836)	3.2 ± 1.6 (n = 7,766)
	$P < 0.001$		$P < 0.001$
	$P < 0.001$		
Pain at rest—all data	1.5 ± 1.0 (n = 3,323)	1.8 ± 1.2 (n = 1,159)	2.5 ± 1.2 (n = 4,507)
	$P < 0.001$		$P < 0.001$
	$P < 0.001$		
Pain with activity—all data	2.7 ± 1.3 (n = 2,585)	3.2 ± 1.4 (n = 677)	4.1 ± 1.7 (n = 3,159)
	$P < 0.001$		$P < 0.001$
	$P < 0.001$		

Data are visual analog scale (VAS) pain scores presented as mean ± SD.

P value represents comparison of intravenous patient-controlled analgesia with opioid (PCA) vs. patient-controlled epidural analgesia (PCEA) and intravenous PCA vs. continuous epidural infusion (CEI) separately (all $P < 0.001$). Individual P values for comparison of CEI with PCEA are shown.

n = weighted number of observations for each parameter; N = actual number of patients per group.

Table 4. Epidural Analgesic Data

Parameter	EA Opioid (N = 287)	EA LA + Opioid (N = 1,262)	EA LA (N = 76)	Intravenous PCA (N = 1,583)	P Values—Intravenous PCA vs.:				
					EAO	EAHY	EALP	EAL/O	EAL
All data	2.5 ± 1.3 (n = 1,024)	2.1 ± 1.3 (n = 6,378)	1.9 ± 0.9 (n = 342)	3.2 ± 1.6 (n = 7,766)	< 0.001	1.0	< 0.001	< 0.001	< 0.001
	$P < 0.001$		$P = 0.21$						
	EA Hydrophilic Opioid (N = 74) 3.0 ± 0.9 (n = 258)								
	$P < 0.001$								
	$P < 0.001$								
	EA Lipophilic Opioid (N = 171) 2.0 ± 1.1 (n = 584)								
	$P = 1.0$								
	$P = 1.0$								
Pain at rest	2.2 ± 1.1 (n = 775)	1.5 ± 1.0 (n = 3,517)	1.2 ± 0.2 (n = 190)	2.5 ± 1.2 (n = 4,507)	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001
	$P < 0.001$		$P = 0.003$						
	EA Hydrophilic Opioid (N = 74) 2.9 ± 0.8 (n = 226)								
	$P < 0.001$								
	$P < 0.001$								
	EA Lipophilic Opioid (N = 171) 1.7 ± 0.9 (n = 418)								
	$P = 0.07$								
	$P < 0.001$								
Pain with activity	3.2 ± 1.4 (n = 249)	2.8 ± 1.3 (n = 2,861)	2.8 ± 0.5 (n = 152)	4.1 ± 1.7 (n = 3,159)	< 0.001	1.0	< 0.001	< 0.001	< 0.001
	$P < 0.001$		$P = 1.00$						
	EA Hydrophilic Opioid (N = 74) 3.8 ± 1.3 (n = 52)								
	$P = 0.003$								
	$P = 0.009$								
	EA Lipophilic Opioid (N = 171) 2.7 ± 1.1 (n = 166)								
	$P = 1.00$								
	$P = 1.00$								

Data presented as mean ± SD. Of the 287 epidural opioid-alone subjects, 171 were classified as lipophilic alone (EALP), 74 were classified as hydrophilic alone (EAHY), and 42 were unspecified.

P value represents comparison of only two groups at one time. Individual P values for comparison between two epidural analgesic regimens are shown. Individual P values for comparisons between intravenous patient-controlled analgesia with opioid (PCA) and one other epidural regimen are shown at right.

EA = epidural; EAL = epidural local anesthetic; EAL/O = epidural local anesthetic + opioid; EAO = epidural opioid (all data combined—includes hydrophilic- and lipophilic-only data); LA = local anesthetic; n = weighted number of observations for each parameter; N = actual number of patients per group.

Table 5. Analgesia by Region of Surgery

Location of Surgery	Epidural Analgesia (N = 1,625)	Intravenous PCA (N = 1,583)	P Value
Thoracic	1.6 ± 1.5 (n = 1,157)	2.7 ± 1.8 (n = 1,139)	< 0.001
Pelvic	2.5 ± 1.2 (678)	3.5 ± 1.5 (655)	< 0.001
Abdominal	2.1 ± 1.2 (4,414)	3.1 ± 1.7 (4,274)	< 0.001
Cesarean delivery	1.8 ± 1.0 (220)	3.0 ± 1.4 (248)	< 0.001
Lower extremity	2.3 ± 1.1 (622)	3.4 ± 1.3 (665)	< 0.001
Multiple	3.1 ± 1.3 (452)	4.2 ± 1.3 (484)	< 0.001

Data are presented as mean ± SD.

n = weighted number of observations for each parameter and includes both rest and incident pain; N = actual number of patients per group; PCA = patient-controlled analgesia with opioid.

publication,¹⁵ which did include a subgroup analysis showing the superior analgesia of epidural analgesia over intravenous PCA, this study is different because the primary focus was on a comparison of intravenous PCA to PCEA and CEI. Despite the fact that there was overlap in articles assessed between the two studies (35 of 50 articles from the current meta-analysis were used in our previous meta-analysis), this new systematic review contains more clinically relevant information for anesthesiologists because it compares intravenous PCA with both CEI and PCEA (*i.e.*, the current study should not be considered a duplicate publication). Many colleagues, both informally and formally,¹⁸ mentioned that our initial analysis¹⁵ was not clinically meaningful for them because the majority of postoperative systemic opioids were delivered *via* intravenous PCA and because there was no differentiation between CEI and PCEA. As such, we decided to undertake a completely new meta-analysis with different inclusion criteria to reflect typical clinical practice.

The results of our meta-analysis corroborate previous systematic reviews of the analgesic efficacy of postoperative epidural analgesia *versus* systemic opioids, which include but are not limited to intravenous PCA with opioids.^{15,16} It may not be surprising that postoperative PCEA and CEI provide significantly superior postoperative analgesia when compared with intravenous PCA with opioids. Unlike that seen with systemic opioids, epidural local anesthetics can block nociceptive input into the central nervous system with the addition of an epidural opioid providing an even greater analgesic ef-

fect.^{20,21} The superior analgesia and physiologic²²⁻²⁴ benefits from epidural analgesia may potentially result in an improvement in perioperative outcomes.²⁵⁻³⁰ In addition, perioperative epidural analgesia may decrease postoperative morbidity (*e.g.*, pulmonary complications, myocardial infarction, gastrointestinal motility) and mortality in high-risk patients, although its effect may not be as apparent for low-risk patients or those undergoing lower-risk procedures.^{11,31-39}

By allowing individualization of postoperative analgesic requirements, intravenous PCA is considered to be the accepted standard by which opioids are delivered to the hospitalized surgical patient. Intravenous PCA provides significantly superior analgesia compared with conventional “as needed” (intravenous, intramuscular, or subcutaneous) opioid administration.^{33,40} Similar to that for intravenous PCA and systemic opioids, PCEA may in one sense be considered the accepted standard for delivery of epidural analgesia. In our analysis, PCEA provided significantly superior analgesia compared with intravenous PCA overall, for each postoperative day, and for pain both at rest and with activity. It was interesting to note that CEI provided superior analgesia *versus* PCEA; however, this may be possibly related to an increase in dose of local anesthetic administered in the CEI group (*i.e.*, subjects receiving PCEA generally use less local anesthetic than those receiving CEI⁴¹), which may be reflected in the higher incidence of motor block for those receiving CEI.

Use of a local anesthetic-based epidural regimen seems to provide the best postoperative pain control

Table 6. Complication Rates

Parameter	Epidural Analgesia				Intravenous PCA	P Value†
	Total	CEI	PCEA	P Value*		
Nausea–vomiting	184/680 (27.6%)	127/419 (30.3%)	57/261 (21.8%)	0.02	211/632 (33.4%)	0.01
Sedation	71/247 (28.7%)	42/136 (30.9%)	29/111 (26.1%)	0.48	91/236 (38.6%)	0.03
Pruritus	190/579 (32.8%)	113/399 (28.3%)	77/180 (42.8%)	0.001	89/519 (17.1%)	< 0.001
Urinary retention	22/203 (10.8%)	19/145 (13.1%)	3/58 (5.2%)	0.13	9/198 (4.5%)	0.02
Motor block	27/320 (8.4%)	19/67 (28.3%)	8/253 (3.2%)	< 0.001	0/65 (0%)	< 0.001

* Continuous epidural infusion (CEI) vs. patient-controlled epidural analgesia (PCEA). † Epidural/total vs. intravenous patient-controlled analgesia with opioid (PCA).

n = actual number of subjects with symptoms; N = actual number of subjects studied for that symptom; Total = aggregate data of CEI + PCEA.

(table 4). Overall, epidural opioid-only regimens seem to provide superior analgesia compared with intravenous PCA but inferior analgesia compared with local anesthetic-based epidural regimens (*i.e.*, VAS values for epidural opioids are intermediate between that for intravenous PCA and local anesthetic-based epidural regimens). However, when analyzed by hydrophilic *versus* lipophilic opioids, the VAS pain scores for epidural hydrophilic opioid-only regimens (delivered primarily *via* a PCA device) were significantly higher than those for lipophilic opioids and local anesthetic regimens and were for the most part equivalent to those for intravenous PCA. As such, hydrophilic opioid-only epidural solutions should not be routinely administered *via* a PCA device for postoperative pain management. In addition, our data also suggest that epidural analgesia would provide superior analgesia compared with intravenous PCA for all types of surgery (table 5). This may be important not only in allowing patients to actively participate in physiotherapy but also in potentially decreasing the incidence of chronic postoperative pain.⁴

The overall complication rates reported are similar to those seen in other sources, although the actual incidence in clinical practice may vary depending on the epidural agent used and how the specific complication is defined. The cumulative incidence of nausea-vomiting from epidural analgesia may be as high as 45–80%,^{42,43} and that for pruritus may be as high as 60%.⁴⁴ However, some large-scale observational PCEA studies note a lower incidence of nausea-vomiting (3.8–14.8%), pruritus (1.8–16.7%), and motor block (0.1–2%) compared with our findings.^{45,46}

There are several limitations to this study, some of which pertain specifically with the issue examined, whereas others relate to the general use of meta-analysis. The clinical significance of our findings despite the presence of a statistical difference is unclear (*i.e.*, is this a clinically meaningful difference?). We were unable to determine the percentage of patients with moderate-severe pain, the percentage of maximum total pain relief, the sum of the pain intensity difference, or the percentage pain intensity difference^{47,48} because of the limitations of available data. In addition, attempting to achieve the lowest possible pain score, a worthy objective *per se*, may not always be the most desirable or only goal of a postoperative analgesic regimen and must be considered in the overall context of what may be sacrificed (*i.e.*, side effects) to achieve this objective. For example, our data suggest that patients receiving CEI have lower pain scores than those receiving PCEA (table 3); however, this superior analgesia may come at a cost (*i.e.*, increased nausea-vomiting and motor block; table 6). In addition, the generalizability of our results to the typical clinical population is difficult to assess, in part because of the protocolization present in randomized trials and the rate of failure or dislodgement of postop-

erative epidural catheters (reported from 6 to 25%^{49–51}), which may limit the analgesic efficacy of epidural analgesia. We also did not weight the quality scoring of the randomized controlled trials used or assess the articles in a blinded fashion because the role of quality assessments in meta-analysis is unclear.^{52–55}

In addition, that there may be discrepancies between meta-analyses and subsequent large randomized controlled trials.⁵⁶ This may be related in part to the presence of publication bias where only positive findings are published primarily in English-language journals.^{57,58} Although we limited our analysis to the English language, only 8 non-English PubMed articles would have qualified for inclusion in our meta-analysis, and the inclusion of these articles (5 studies [n = 395 out of 514 subjects total] of which showed that epidural analgesia produced superior analgesia *vs.* intravenous PCA) would not have changed our results. The effect of excluding non-English trials on the results of a meta-analysis is equivocal, with some data suggesting that exclusion of trials published in non-English may actually result in a more conservative estimate of the treatment effect.⁵⁹

In summary, we performed a meta-analysis of randomized controlled trials to determine the analgesic efficacy of postoperative epidural analgesia compared with intravenous PCA with opioids. Epidural analgesia provided a statistically and clinically significant improvement in postoperative pain control compared with intravenous PCA with opioids—regardless of analgesic regimen (local anesthetic with or without opioid or opioid alone), type of epidural analgesia (CEI *vs.* PCEA), site of surgical incision, or measured pain outcomes (rest or incident pain), with the exception of hydrophilic opioid-only regimens. CEI provided statistically superior (although not necessarily clinically superior) postoperative analgesia *versus* PCEA, but with a higher incidence of nausea-vomiting and motor block. Our results suggest that postoperative PCEA and CEI may provide significantly superior analgesia when compared with intravenous PCA, the accepted standard for delivery of postoperative opioids. These analgesic benefits, along with other potential benefits,^{60–65} should be weighed against the risks^{66–71} of epidural analgesia when considering the route of delivery for postoperative analgesia, and the balance between these risks and benefits should be determined for each surgical patient.⁷² When feasible, clinicians may also consider using PCEA with a local anesthetic-based solution over CEI to minimize analgesic-related side effects while providing superior postoperative analgesia compared with intravenous PCA with opioids.

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Stephen Barratt, Ph.D., F.A.N.Z.C.A. (Consultant, Department of Anesthesia

and Pain Management, Royal North Shore Hospital, St. Leonards, Australia); Honorio Benzon, M.D. (Professor of Anesthesiology, Department of Anesthesiology, Northwestern University Feinberg School of Medicine, Chicago, Illinois); Xavier Capdevila, M.D., Ph.D. (Professor, Department of Anesthesiology, Lapeyronie University Hospital, Montpellier, France); Phoon P. Chen, M.D., F.H.K.A.M. (Honorary Associate Professor, Department Anesthesia and Intensive Care, Chinese University of Hong Kong, Hong Kong, SAR of China); David Cooper, F.R.C.A. (Consultant Anesthetist, James Cook University Hospital, Middlesbrough, United Kingdom); Rob Dyer, F.C.A. (SA) (Senior Specialist, Department of Anesthesia, Groote Schuur Hospital, Cape Town, South Africa); Charles Fisher, M.D., M.H.Sc., F.R.C.S.C. (Department of Orthopaedics, Vancouver Hospital and Health Sciences Centre, Vancouver, Canada); Per Flisberg, M.D., Ph.D. (Consultant, Department of Anesthesia and Pain Medicine, Royal Perth Hospital, Perth, Australia); Johan Lundberg, M.D., Ph.D. (Adjunct Professor of Anesthesiology, Dartmouth Medical School, Hanover, New Hampshire); Edward Norris, M.D. (Associate Professor, Department of Anesthesiology and Critical Care Medicine, The Johns Hopkins University, Baltimore, Maryland); Mark Priestley, M.B.B.S., F.A.N.Z.C.A. (Consultant, Department of Anesthesia, Westmead Hospital, Westmead, Australia); Yehuda (Udi) Shavit (Professor, Department of Psychology, Hebrew University, Jerusalem, Israel); Eugene Viscusi, M.D. (Associate Professor, Department of Anesthesiology, Jefferson Medical College, Thomas Jefferson University, Philadelphia, Pennsylvania); and Avi Weinbroum, M.D. (Director, Post-Anesthesia Care Unit and Animal Research Laboratory, Tel Aviv Sourasky Medical Center, Tel Aviv, Israel).

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Appendix: Included Articles

1. Allaire PH, Messick JM Jr, Oesterling JE, Byer DE, Myers RP, Lieber MM, Chantigian RC, Welna JO, Patterson DE, Blute ML: A prospective randomized comparison of epidural infusion of fentanyl and intravenous administration of morphine by patient-controlled analgesia after radical retropubic prostatectomy. *Mayo Clin Proc* 1992; 67:1031-41

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