Efficacy of Continuous Wound Catheters Delivering Local Anesthetic for Postoperative Analgesia: A Quantitative and Qualitative Systematic Review of Randomized Controlled Trials

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Effective postoperative analgesia is important from the patient's perspective and can also improve clinical outcomes.[1] Recent surveys report only modest success in providing suitable analgesia, as 30% to 86% of surgical patients report moderate to severe pain after a surgical procedure.[2,3] Although "advanced" analgesic techniques, such as epidural analgesia or perineural catheters, can provide superior analgesia, many of these analgesic modalities are labor-intensive and expensive.[4,5] A promising modality that might help improve postoperative analgesia is the relatively simple technique in which the surgeon directly places a catheter to infuse local anesthetic into wounds at the end of the procedure. This modality can be widely used, is technically efficient, offers the potential to provide complete analgesia or to substantially reduce the need for opioids and their related side effects, can be used for several days, and can now, with the introduction of new portable pumps, be used on an ambulatory basis.[6] Although there are multiple reports and small randomized controlled trials (RCTs) examining use of continuous wound catheters in multiple surgical procedures, there have been conflicting reports of the overall efficacy, and no single, large RCT has definitively assessed the risk benefit of this modality. We conducted this systematic review of randomized trials to determine the efficacy of this modality.

Competing Interests Declared: None.

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METHODS

Literature review

The National Library of Medicine's Medline database and the Cochrane Central Register of Controlled Trials were searched for the time period January 1, 1966 to February 19, 2006. Two authors (SSL and JMR) performed independent searches. Search strategies included combining "postoperative pain," "postoperative analgesia," or "postoperative period" and "local Anesthetics." This combined search was then refined by combining "and" with "continuous," "infusion," "perfusion," "irrigation," "instillation," or "patient controlled." Another search was performed by combining "local anesthetics" and "wounds," "intraarticular," or "subcutaneous." A third search was performed by combining "catheters" and "local anesthetics," "wound," "continuous," "infiltration," "regional anesthesia," or "pain." Searches were restricted to "adults" (older than 18 years of age) and "clinical trials" or "randomized controlled trial." No language restriction was used. This final search identified 594 potential RCTs for systematic review.

Inclusion criteria

All abstracts were reviewed for potential inclusion in the systematic review. Only prospective RCTs that assessed either visual analogue pain scores or opioid consumption were included. Only RCTs that used continuous wound catheters placed by the surgeon into the operative field were included. RCTs that reported data as only mean or median values could be included in the qualitative review but not in the quantitative review (meta-analysis) because of unusable data.

Exclusion criteria

All RCTs that used continuous peripheral nerve block and central neuraxial (epidural or spinal) catheter techniques were excluded. Recent metaanalyses have already analyzed these techniques, and we did not consider them

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to qualify as wound catheters per inclusion criteria.[4,5] All RCTs that did not specify a placebo solution (saline or water) delivered through the wound catheter, placebo nonfunctional pump, or a no-catheter control group were excluded. RCTs with a study infusion period of less than 24 hours postoperatively were excluded. RCTs with unusual study designs were excluded (eg, local anesthetic injected through wound drain and then drained out of wound).

Data extraction and analysis

Each study's methodology and results were recorded. Quality of individual RCTs was quantified by the Jadad scale.[7] Data were extrapolated from figures as needed. Definition of outcomes and criteria for opioid rescue and hospital discharge were recorded as originally defined by the study. Specific outcomes that were extracted included pain scores at rest and with activity. Pain scores were averaged to create a single mean visual analogue score (VAS) for each RCT for the duration of local anesthetic infusion. This was separately performed for scores at rest and with activity. We extracted incidence of need for opioid rescue during the study and calculated the amount of opioid spared as equivalents of IV morphine (mg) per day. The only opioid-related side effect (eg, nausea and vomiting, sedation, or pruritus) that was reported with any frequency was nausea and vomiting. Incidences of postoperative nausea and vomiting (PONV) were extracted. Patient satisfaction was quantified with a variety of measures, and we extracted the most prevalent (incidence of patients rating their satisfaction as "excellent"). Duration of hospital stay was extracted. Incidences of catheter-related complications (wound infections and clinical systemic toxicity from local anesthetics) were extracted. Incidences of catheter or pump failure were extracted. Two authors (SSL and JMR) independently performed data extraction and resolved any discrepancies together. RCTs were subdivided into the following clinical surgical groups for subanalysis: cardiothoracic surgery, general surgery, gynecology-urology surgery, and orthopaedic surgery.

Statistical analysis

Quantitative systematic review was done with metaanalysis. The level of significance for all tests was set at a $p = 0.05$ and variances were not assumed to be equal. For dichotomous outcomes, study results were pooled and odds ratios calculated with the Mantel-Haenszel method. Odds ratios with 95% confidence intervals are displayed for the effect statistic. For continuous outcomes, study results were pooled and means and standard deviations calculated with the inverse variance method. Weighted mean differences and 95% confidence intervals are displayed for the effect statistic. Heterogeneity was analyzed using the I^2 and Q statistics. If heterogeneity was significant ($p < 0.05$), then a random effects model was used. Otherwise, a fixed effect model was used. All statistical analyses were performed with Review Manager 4.2 (The Cochrane Collaboration's Information Management System; Nordic Cochrane Centre Rigshospitalet). A funnel plot of the primary outcomes (VAS at rest) was examined for potential bias. A qualitative systematic review was also planned on all included RCTs. This consisted of noting study characteristics and outcomes in a table format.

RESULTS

Quantitative systematic review (metaanalysis)

Forty-four RCTs enrolling a total of 2,141 patients were included for final quantitative analysis. Reasons for exclusion are indicated in Figure 1.[8-51] Seven RCTs that reported data only as mean or median values were excluded from metaanalysis, but included in the following qualitative review. The included RCTs were published between 1983 and 2006, with most in the past decade ($n = 34$), were small in size (number of enrolled subjects ranged from 16 to 100), and primarily used bupivacaine ($n = 34$) or ropivacaine ($n = 9$) ranging from 0.2% to 0.5% for the local anesthetic. Wound catheters were placed in a variety of locations (subcutaneous, suprafascial, subfascial, intraarticular, peripleural, and periosteal), and all but two RCTs specifically stated that catheters were not placed or activated until surgical closure, so no preemptive analgesia was attempted. Local anesthetic was infused for a median and mode of 2 days. The cardiothoracic subgroup had the most RCTs ($n = 14$), followed by orthopaedics ($n = 12$), general surgery ($n = 11$), and gynecology-urology ($n = 7$). Median Jadad score was 4 and mode was 4.

Metaanalysis associated multiple potential benefits with use of continuous wound catheters (Table 1). For all groups combined, mean VAS pain scores decreased considerably at rest (−10 mm weighted mean difference; 95% CI, −13 to −7 mm) and with activity (−22 mm weighted mean difference; 95% CI, −32 to −13 mm). Subgroup analysis confirmed decreased pain

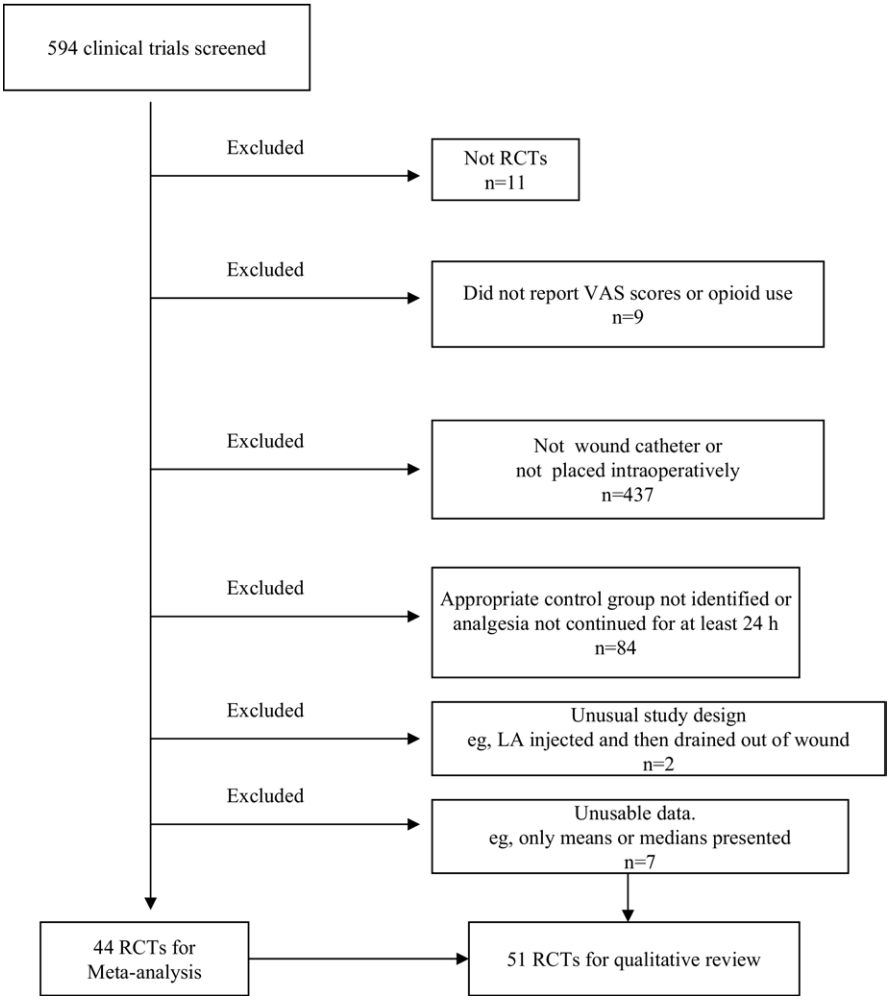

Figure 1. Flow diagram of exclusion of clinical trials for metaanalysis and for qualitative review. LA, local anesthetic group; RCT, randomized controlled trial; VAS, visual analogue scale.

scores. Figure 2 displays metaanalysis of VAS scores at rest for combined and subgroup data. For all groups combined, both need for opioid rescue (41% versus 66%; odds ratio, 0.15; 95% CI) and daily consumption of opioids (−11 mg per day weighted mean difference; 95% CI, −14 to −7 mg) were substantially reduced in the continuous wound catheter group. Subgroup analyses indicated considerably less rescue in all surgery groups and less need for opioid in all groups except orthopaedics. Figure 3 displays metaanalysis for opioid use for combined and subgroup data. For all groups combined, incidence of PONV was reduced in the continuous wound catheter group (24% versus 40%; odds ratio, 0.45; 95% CI, 0.08 to 0.3). Although all subgroups had lower incidences of PONV for the continuous wound catheter groups, only general and gynecology-urology groups reached individual statistical significance. For all groups combined, percent of patients rating their analgesia as "excellent" was low overall, but greater in the continuous wound catheter group (43% versus 13%; odds ratio, 7.7; 95% CI, 1.8 to 34). Orthopaedic surgery was the subgroup with the most "excellent" patient satisfaction with continuous wound catheters (92%) versus control group (27%). For all groups combined, length of hospital stay was reduced by a day in the continuous wound catheter group (7 versus 8 days), which was also significant ($p<0.05$) in the cardiothoracic and orthopaedic surgery subgroups. For all groups combined, reported wound infection rates were similar between catheter with local anesthetic (0.7%) and catheter with placebo or no-catheter control groups (1.2%). No cases of systemic toxicity from local an-

Table 1. Effects of Continuous Wound Catheters on Postoperative Outcomes

Outcomes	n	No. of trials	Wound catheter with local anesthetic*	Control*	WMD† (95% CI)	OR† (95% CI)	p Value
VAS pain score at rest (mm)							
All groups combined	1,814	39	26	38	−10 (−13 to −7)		< 0.001
Cardiothoracic	521	12	29	35	−11 (−15 to −6)		< 0.001
General	573	10	31	39	−9 (−17 to −1)		0.02
Gynecology-urology	262	5	25	29	−7 (−10 to −5)		< 0.001
Orthopaedics	458	12	23	40	−14 (−21 to −8)		< 0.001
VAS pain score with activity (mm)							
All groups combined	794	16	36	50	−15 (−22 to −9)		< 0.001
Cardiothoracic	83	1	33	39	−6 (−13 to 1)		0.1
General	164	3	34	39	−7 (−24 to 10)		0.42
Gynecology-urology	226	4	39	49	−13 (−22 to −4)		0.006
Orthopaedics	321	8	36	58	−22 (−32 to −13)		< 0.001
Opioid rescue during infusion period (%)							
All groups combined	411	9	41	66		0.15 (0.08−0.29)	< 0.001
Cardiothoracic	0	0					
General	237	5	47	63		0.17 (0.07−0.47)	< 0.001
Gynecology-urology	86	2	44	95		0.06 (0.01−0.24)	< 0.001
Orthopaedics	88	2	22	42		0.2 (0.05−0.82)	0.02
Opioid use per day as mg IV morphine equivalents (mg)							
All groups combined	1,637	37	17	28	−11 (−14 to −7)		< 0.001
Cardiothoracic	518	13	23	34	−12 (−19 to −6)		< 0.001
General	369	7	19	32	−12 (−19 to −6)		< 0.001
Gynecology-urology	342	6	26	36	−9 (−14 to −4)		0.001
Orthopaedics	408	11	8	18	−8 (−19 to 2)		0.12
PONV (%)							
All groups combined	614	13	24	40		0.45 (0.3−0.68)	< 0.001
Cardiothoracic	56	2	24	27		0.71 (0.2−2.6)	0.6
General	211	3	32	46		0.47 (0.24−0.89)	0.02
Gynecology-urology	146	3	19	53		0.15 (0.06−0.4)	0.01
Orthopaedics	201	5	21	27		0.68 (0.34−1.37)	0.28
Patients rating satisfaction as excellent (%)							
All groups combined	209	5	43	13		7.7 (1.8−34)	0.007
Cardiothoracic	0	0					
General	50	1	4	4		1 (0.1−17)	1
Gynecology-urology	86	2	26	7		4.1 (0.5−34)	0.19
Orthopaedics	73	2	92	27		26 (6−109)	< 0.001
Length of stay in hospital (d)							
All groups combined	753	15	7	8	−1 (−2 to −0.3)		0.04
Cardiothoracic	263	6	9	10	−1 (−1.9 to −0.1)		0.04
General	190	3	8	8	−0.04 (−1.5 to −1.4)		0.05
Gynecology-urology	226	4	4	4	−0.3 (−0.8 to 0.3)		0.3
Orthopaedics	74	2	6	8	−2.5 (−2.8 to −2.1)		< 0.001

A total of 44 randomized controlled trials with 2,141 patients were included for metaanalysis.
*Weighted by subject number.
†Weighted by inverse variance.
OR, odds ratio; PONV, postoperative nausea and vomiting; VAS, visual analogue score; WMD, weighted mean difference.

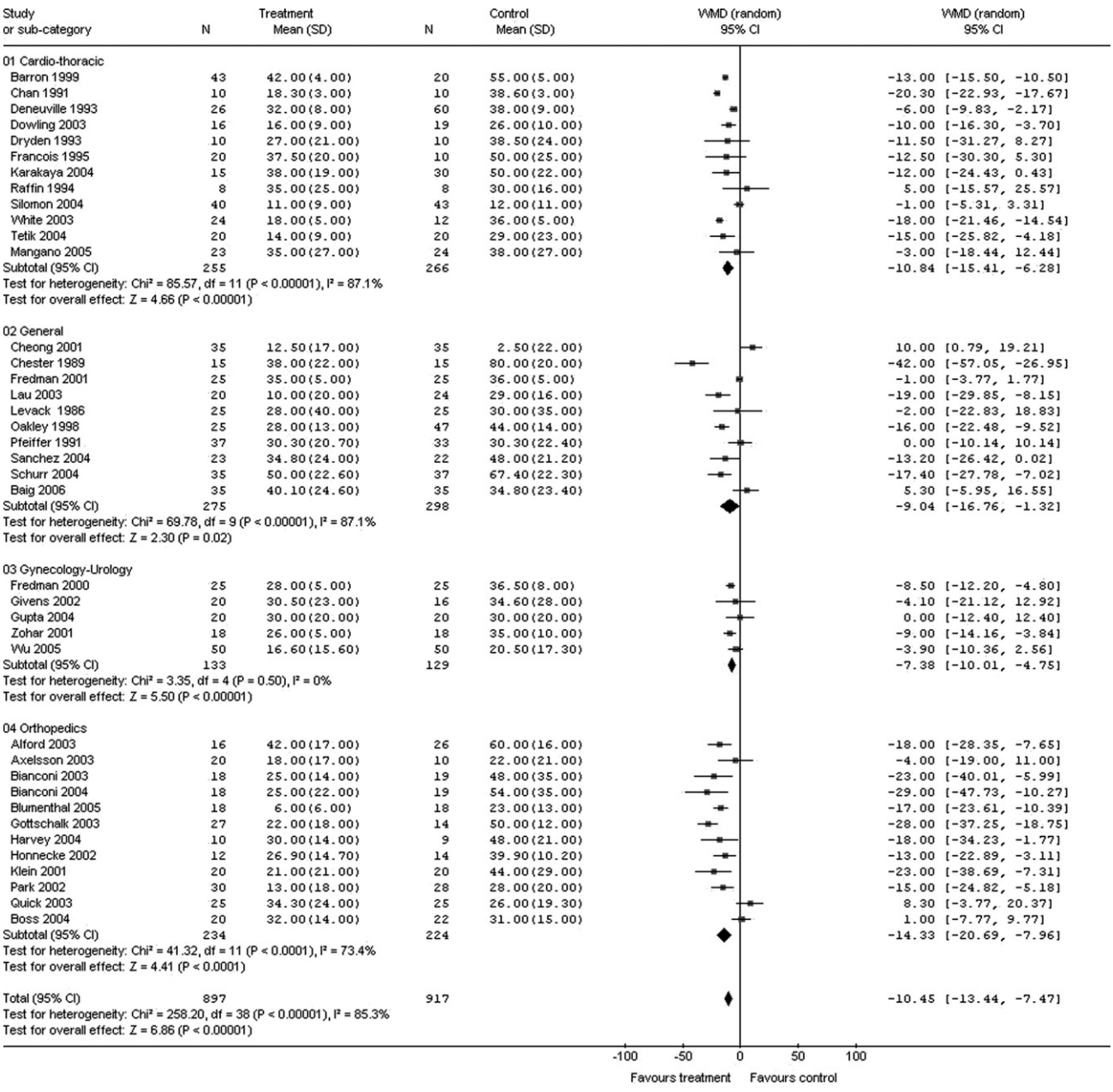

Figure 2. Summary visual analogue scale (VAS) score for pain intensity at rest (0 to 100) for subgroups and for all groups combined. A weighted mean difference (WMD) < 0 indicates less pain with treatment (wound catheter with local anesthetic) compared with control. When the 95% CI does not include 0, the difference is considered statistically significant.

esthetics were reported. Incidence of reported catheter or pump failure was 1.1%. Because of the low incidences of these complications, no subgroup analyses were performed. Examination of the funnel plot of primary outcomes of VAS score at rest (Fig. 4) did not indicate publication or other types of bias, as the plot is symmetrical at the base and tapers with increasing precision and sample size at the top.

Qualitative systematic review

All RCTs from the metaanalysis were included in the qualitative review. In addition, seven RCTs excluded from metaanalysis because of presentation of only mean or median values were included in the qualitative review (Fig. 1) and are specifically noted in Tables 2 to 5.[52-58] A total of 51 RCTs with 2,407 subjects are included for qualitative review.

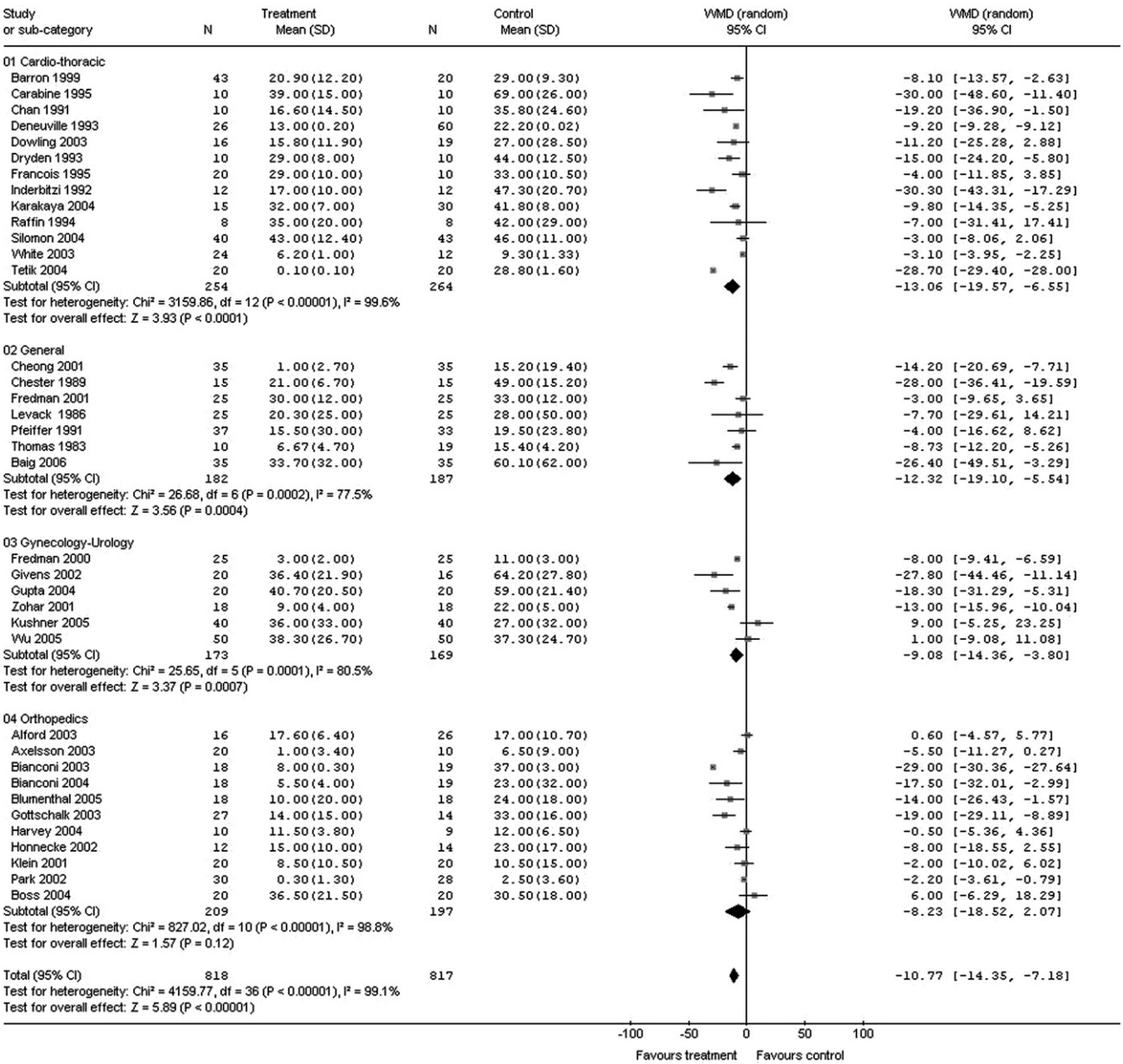

Figure 3. Opioid use (milligrams of morphine per day) for subgroups and all groups combined. A weighted mean difference (WMD) < 0 indicates less pain with treatment (wound catheter with local anesthetic) compared with control. When the 95% CI does not include 0, the difference is considered statistically significant.

Thirteen of these RCTs acknowledged sponsorship from industry.

Cardiothoracic surgery

Most trials (n = 11) examined thoracotomy for lung resection, with the exception of 1 examining thoracotomy for esophagectomy and 3 examining median sternotomy for cardiac surgery (Table 2). Only continuous infusion or intermittent bolus delivery was studied. Thoracotomy wound catheters were placed in a variety of described peripleural locations (two extrapleural, two interpleural, three intercostal, and four intrapleural). Two cardiac studies placed catheters adjacent to the sternum and the other placed subfascial and subcutaneous (SC) catheters. Nearly all RCTs (12 of 14) reported significant ($p<0.05$) analgesic efficacy for either pain

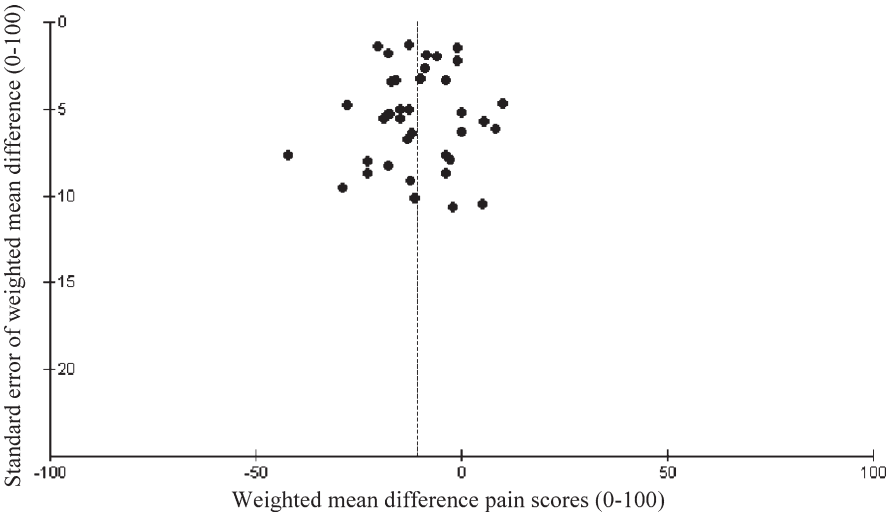

Figure 4. Funnel plot of pooled effect of reduction in pain scores (X axis) versus estimate of precision (standard error of weighted mean difference) on Y axis. Each dot represents an individual randomized controlled trial. The dots are centered on the weighted mean difference of a reduction in pain scores of 12 (0 to 100) with continuous wound catheters. The plot is symmetrical at the base and tapers at the top as precision increases. This symmetrical shape suggests a lack of bias in the data.

scores or opioid use. Pain scores in the immediate postoperative period were considerably reduced in 11 of 13 RCTs, and 5 RCTs reported reduction through postoperative day 2. Few trials reported opioid-related side effects (3 of 14) or patient satisfaction (1 of 14). Six trials reported length of stay, with four of six noting some reduction in the wound catheter group.

General surgery

A variety of surgical procedures, including upper abdominal and vascular surgery, were used (Table 3). A variety of continuous delivery methods were used, including patient-controlled analgesia, continuous infusion, and intermittent bolus. Wound catheters were placed SC, subfascial, or between peritoneum and muscle. Most RCTs (10 of 12) reported significant ($p<0.05$) analgesic efficacy as either reduced opioid use or reduced pain scores. Pain scores in the immediate postoperative period were substantially reduced in 8 of 11 RCTs, but only 3 RCTs reported reduction through postoperative day 2. Few trials reported opioid side effects (4 of 12), patient satisfaction (2 of 12), or length of hospital stay (3 of 12).

Gynecology-urology surgery

Most RCTs examined either cesarean section or abdominal hysterectomy (Table 4). A variety of continuous delivery methods were used, including patient-controlled analgesia, continuous infusion, and intermittent bolus. The majority of wound catheters were placed between muscle fascia and SC tissue (six of nine). The slight majority (five of nine) of RCTs reported substantial analgesic efficacy, either as reduced pain scores or reduced opioid use. Pain scores in the immediate postoperative period were substantially reduced in four of nine RCTs, with no RCTs reporting reduction past postoperative day 1. All RCTs that reported side effects[3] and patient satisfaction[2] found improvement with wound catheters. Only five RCTs reported length of stay without any differences.

Orthopaedic surgery

A variety of surgical procedures were studied, including open and arthroscopic procedures on upper and lower extremities and spine surgery (Table 5). A variety of continuous delivery methods were used, including patient-controlled analgesia, continuous infusion, and intermittent bolus. A variety of locations were used for the wound catheters, including intraarticular, SC, and periosteal. Almost all RCTs (13 of 16) reported significant ($p<0.05$) analgesic efficacy either as reduced pain scores or opioid use. Pain scores in the immediate postoperative period were significantly ($p<0.05$) reduced in 12 of 16 RCTs, and 11 RCTs reported reduction through postoperative days 2 to 5. Relatively few trials

Table 2. Randomized Controlled Trials in Cardiothoracic Surgery

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Barron,[14] 1999	Thoracotomy	Extraplural catheter with 0.25% bupiv 0.1 mL/kg/h for 72 h, n = 22 1% lidocaine via catheter, n = 21 Saline via catheter, n = 20 Rescue: morphine IV PRN	Decreased through 80 h, $p < 0.01$	Decreased by 27%, $p < 0.05$	NA	NA	8.3 versus 9.6 d	Jadad score = 2
Carabine,[15] 1995	Thoracotomy	Extrapleural catheter with 0.25% bupiv 5 mL/h for 24 h, n = 10 No catheter, IV PCA morphine, n = 10 Rescue: morphine IV PCA	Decreased at rest and activity through 24 h, $p < 0.03$	Decreased by 43%, $p < 0.006$	10% versus 20%	NA	NA	Pain scores excluded from metaanalysis as only median values were presented Jadad score = 2
Chan,[16] 1991	Thoracotomy	2 intercostal catheters with 0.5% bupiv + 1:200,000 epinephrine q 6 h for 24 h, n = 10 Saline via catheter, n = 10	Decreased through 24 h, $p < 0.05$	Decreased by 53%, $p < 0.05$	NA	NA	NA	Jadad score = 3
Deneuville,[17] 1993	Thoracotomy	Intercostal catheter with 0.5% bupiv 3 mL/h for 5 d, n = 26 Saline via catheter, n = 26 No catheter, buprenorphine IM PRN, n = 34 Rescue: buprenorphine IM PRN	Decreased for POD 0, $p < 0.02$	Decreased by 41%, $p < 0.001$	NA	NA	NA	Jadad score = 3
Dowling,[18] 2003	Coronary artery bypass	2 catheters anterior to sternum with 0.2% ropiv 4 mL/h for 48 h, n = 16 Saline via catheter, n = 19 Rescue: morphine IV PCA	Decreased through 72 h, $p < 0.02$	Decreased by 46%, $p < 0.04$	NA	NA	5.2 versus 8.2 d, $p = 0.001$	Jadad score = 5
Dryden,[19] 1993	Thoracotomy	2 intercostal catheters with 0.25% bupiv 5 mL/h for 24 h, n = 10 Saline via catheters, n = 10 Rescue: morphine IV PCA	Decreased through 48 h, $p = 0.03$	Decreased by 34%, $p = 0.04$	Equivalent nausea scores	NA	NA	Crossover design Jadad score = 5
Francois,[20] 1995	Esophagectomy	2 interpleural catheters with 1 mg/kg 0.5% bupiv + 1:200,000 epinephrine q 4 h for 2 d, n = 10 2% lidocaine with epinephrine via catheters, n = 10 Saline via catheters, n = 10 Rescue: morphine IV PCA	Decreased through 32 h, $p < 0.05$	Decreased by 12%, $p < 0.02$	NA	NA	NA	Jadad score = 4
Inderbitzi,[21] 1992	Thoracotomy	Intrapleural catheter with 0.5% bupiv 10 mL/h for 48 h, n = 12 Saline via catheter, n = 12 Rescue: nicomorphine IV PRN	NA	Decreased by 64%, $p < 0.01$	NA	NA	NA	Jadad score = 2

(continued)

Table 2. Continued

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Karakaya,[22] 2004	Thoracotomy	Interpleural catheter with 0.25% bupiv + epinephrine 1:200,000 20 mL q 6 h for 48 h, n = 15 Saline via catheter, n = 15 Noncatheter, fentanyl IV PCA, n =15 Rescue: fentanyl IV PCA	Decreased through 12 h, $p < 0.05$	Equivalent	NA	NA	8 versus 9 days	15 patients randomized to interpleural analgesia with bupivacaine/ fentanyl/epinephrine via catheter excluded from metaanalysis because of mixed mechanisms of analgesia Jadad score = 1
Magnano,[50] 2005	Cardiac surgery via median sternotomy	Catheter anterior to sternum with 0.5% bupiv 5 mL/h for 36 h, n = 23 Saline via catheter, n = 24 Rescue: morphine IV PRN	Equivalent	Equivalent	NA	NA	NA	Opioid use not used in metaanalysis as only means were displayed. Jadad score = 1
Raffin,[23] 1994	Thoracotomy	Interpleural catheter with 2% lidocaine + epinephrine 1:200,000 0.05 mL/kg/h for 48 h, n = 8 Saline via catheter, n = 8 Rescue: morphine IV PCA	Decreased for 1st hour otherwise equivalent, $p < 0.05$	Decreased by 17%, $p < 0.05$	NA	NA	18.4 versus 17.5 d	Jadad score = 5
Silomon,[24] 2000	Thoracotomy	Interpleural catheter with 0.5% bupiv 20 mL q 4 h for 36 h, n = 40 Saline via catheter, n = 43 Rescue: piritramide IV PCA	Equivalent	Equivalent	NA	NA	12 versus 12 d	Jadad score = 4
Tetik,[25] 2004	Thoracotomy	Intrapleural catheter with 0.25% bupiv 40 mL q 6 h for 24 h, n = 20 Saline via catheter, n = 20 Rescue: diclofenac IM	Decreased for first 6 h, $p < 0.001$	Deceased by 99%, Not analyzed	NA	NA	Equivalent without specifics provided	Length of stay excluded from metaanalysis as no numeric values were presented Jadad score = 1
White,[26] 2003	Cardiac surgery via median sternotomy	1 subfascial catheter and 1 subcutaneous catheter with 0.25% bupiv at 2 mL/h for 48 h, n = 12 0.5% bupiv via catheters, n = 12 Saline via catheters, n = 12 Rescue: morphine IV PCA	Decreased through 72 h, $p < 0.05$	Decreased by 33%, $p < 0.05$	29% versus 36%	Increased, $p < 0.05$	4.6 versus 5.7 d	Patient satisfaction excluded from metaanalysis due to type of data presentation Jadad score = 4

All 14 trials and 565 patients were included in qualitative review and metaanalysis.
Bupiv, bupivacaine; LA, local anesthetic group; NA, not available; PCA, patient-controlled analgesia; POD, postoperative day; PONV, postoperative nausea and vomiting; PRN, pro re nata; Ropiv, ropivacaine.

Table 3. Randomized Controlled Trials in General Surgery

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Baig,[48] 2006	Colectomy	2 subcutaneous catheters with 0.5% bupiv 4 mL/h for 72 h, n = 35 Saline via catheter, n = 35 Rescue: morphine IV PCA	Decreased on POD 2, otherwise equivalent	Decreased by 43%, $p < 0.04$	63% versus 71%	NA	10 versus 10 d	Jadad score = 4
Cheong,[8] 2001	Colorectal	Subcutaneous catheter with 0.5% bupiv 2 mL/h for 60 h, n = 35 No catheter, IV PCA morphine, n = 35 Rescue: morphine subcutaneous for catheter	Decreased on POD 1, otherwise equivalent	Decreased by 93%, $p < 0.001$	6% versus 17%	NA	5 versus 6 d	Jadad score = 1
Chester,[9] 1989	Cholecystectomy	Catheter between peritoneum and rectus with 0.5% bupiv 4 mL/h for 24 h, n = 15 Saline via catheter, n = 15 Rescue: meperidine IV PCA	Decreased through 24 h, $p < 0.001$	Decreased by 57%, $p = 0.01$	NA	NA	NA	Crossover design Jadad score = 4
Fredman,[10] 2001	Major abdominal	2 subcutaneous catheters with 0.25% bupiv PCA for 24 h, n = 25 Water via catheter, n = 25 Rescue: meperidine IV/IM PRN for both	Equivalent	Equivalent	Equivalent	Equivalent nausea scores	9 versus 9 d	Jadad score = 4
Lau,[32] 2003	Inguinal hernia	Subfascial catheter with 0.5% bupiv 2 mL/h for 48 h, n = 20 No catheter, n = 24 Rescue: diclofenac/propoxyphene/ paracetamol po PRN	Decreased with rest and activity through POD 1, $p < 0.01$	Equivalent	NA	NA	Ambulatory surgery	Jadad score = 1
LeBlanc,[52] 2005	Inguinal hernia	Subfascial catheter with 0.5% bupiv 2 mL/h for 48 h, n = 29 Saline via catheter, n = 23 Rescue: hydrocodone po PRN	Equivalent	Decreased by 70%, $p < 0.05$	NA	NA	Ambulatory surgery	Excluded from metaanalysis as only mean values were presented Jadad score = 4
Levack,[11] 1986	Cholecystectomy splenectomy	Catheter between peritoneum and muscle with 0.5% bupiv 10 mL bid for 3 d, n = 25 Saline via catheter, n = 25 Rescue: methadone	Decreased through 80 h, $p < 0.05$	Decreased by 29%, $p < 0.05$	NA	NA	NA	Jadad score = 1
Oakley,[33] 1998	Inguinal hernia	Subfascial catheter with 0.5% bupiv 2 mL/h for 50 h, n = 25 Saline via catheter, n = 24 No catheter, n = 23 Rescue: aspirin/paveretum po PRN	Decreased through POD 2, $p < 0.04$	Equivalent	NA	NA	Ambulatory surgery	Opioid use excluded from metaanalysis as only median values were presented Jadad score = 1

(continued)

Table 3. Continued

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Pfeiffer,[12] 1991	Abdominal aortic aneurysm	2 catheters subcutaneous or submuscular 0.5% bupiv 40 mL qid for 48 h, n = 37 Saline via catheter, n = 33 Rescue: morphine IM PRN	Equivalent	Equivalent	NA	NA	NA	Jadad score = 2
Sanchez,[34] 2004	Inguinal hernia	Subcutaneous catheter with 0.25% bupiv 2 mL/h for 48 h, n = 23 Saline via catheter, n = 22 Rescue: hydrocodone	Decreased on POD 2–5, $p < 0.05$	Equivalent	NA	NA	Ambulatory surgery	Opioid use was excluded from metaanalysis as no mg dose of hydrocodone was presented Jadad score = 4
Schurr,[35] 2004	Inguinal hernia	Subfascial catheter with 0.5% bupiv 2 mL/h for 60 h, n = 35 Saline via catheter, n = 37 Rescue: hydrocodone/acetaminophen po PRN	Decreased through POD 1, $p < 0.05$	Equivalent	26% versus 49%	Equivalent nausea scores	Ambulatory surgery	Opioid use excluded from metaanalysis as only mean values were presented Jadad score = 5
Thomas,[13] 1983	Cholecystectomy	Catheter between peritoneum and muscle with 0.5% bupiv 10 mL q 4 h for 48 h, n = 10 Saline via catheter, n = 9 No catheter, n = 10 Rescue: papaveretum PRN	NA	Decreased by 57%, $p < 0.01$	NA	NA	NA	Jadad score = 3

Twelve trials with 654 patients were included in qualitative review and 11 trials with 602 patients were included in metaanalysis.
Bupiv, bupivacaine; LA, local anesthetic group; NA, not available; PCA, patient-controlled analgesia; PONV, postoperative nausea and vomiting; PRN, pro re nata; Ropiv, ropivacaine.

Table 4. Randomized Controlled Trials in Gynecologic and Urologic Surgery

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Fredman,[27] 2000	Cesarean section	Catheter above fascia with 0.2% ropiv PCA for 24 h, n = 25 Saline via catheter, n = 25 Rescue: morphine IV/dipyrone po PRN	Decreased only with activity for first 6 h, otherwise equivalent, $p < 0.04$	Decreased by 73%, $p < 0.01$	NA	Increased, $p = 0.001$	5 versus 5 d	Jadad score = 4
Givens,[28] 2002	Cesarean section	2 catheters above fascia with 0.25% bupiv 4 mL/h for 48 h, n = 20 Saline via catheters, n = 16 Rescue: morphine IV PCA	Equivalent	Decreased by 43%, $p < 0.01$	NA	NA	NA	Jadad score = 4
Gupta,[29] 2004	Abdominal hysterectomy	Intraperitoneal catheter with 0.25% levobupivacaine 5 mL/h for 24 h, n = 20 Saline via catheter, n = 20 Rescue: ketobemidone IV PCA	Decreased for first 2 h, otherwise equivalent, $p < 0.05$	Decreased by 31%, $p < 0.03$	15% versus 50%, $p < 0.03$	NA	4 versus 4 d	Jadad score = 4
Kristensen,[53] 1999	Abdominal hysterectomy	2 supraperitoneal catheters with 0.25% bupiv 15 mL q 4 h for 48 h, n = 22 Saline via catheter, n = 19 Rescue: morphine IV PRN	Equivalent	Equivalent	NA	NA	NA	Excluded from metaanalysis as only mean values were presented Jadad score = 4
Kushner,[49] 2005	Mixed gynecologic oncology	Catheter in subcutaneous layer with 0.5% bupiv 2 mL/h for 72 h, n = 40 Saline via catheter, n = 40 Rescue: morphine or hydromorphone IV PCA	Equivalent	Equivalent	NA	NA	4.4 versus 5.3 d	Pain scores excluded from metaanalysis as only mean values were presented Jadad score = 5
Leong,[54] 2002	Abdominal hysterectomy	Catheter between muscle fascia and subcutaneous with 0.5% bupiv 2 mL/h for 48 h, n = 26 Saline via catheter, n = 26 Rescue: morphine IV PCA	Equivalent	Equivalent	NA	NA	NA	Excluded from metaanalysis as no numeric values for VAS and only mean values for opioid use were presented Jadad score = 1
Mecklem,[30] 1995	Cesarean section	Catheter between muscle fascia and subcutaneous with 0.25% bupiv 20 mL q 6 h for 44 h, n = 35 Saline via catheter, n = 35 Rescue: morphine IV PCA	Decreased for POD 1, otherwise equivalent, $p < 0.05$	Decreased by 25%, $p < 0.05$	9% versus 31%	NA	NA	Pain scores and opioid use excluded from metaanalysis as only mean values were presented Jadad score = 4

(continued)

Table 4. Continued

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Wu,[51] 2005	Radical retropubic prostatectomy	Catheter beneath rectus muscle fascia with 0.5% bupivacaine 2 mL/h until patient discharge on postoperative day 3, n = 50 Saline via catheter, n = 50 Rescue: hydromorphone IV PCA	Equivalent	Equivalent	NA	NA	3.2 versus 3.1 d	Jadad score = 4
Zohar,[31] 2001	Abdominal hysterectomy	Catheter above fascia with 0.25% bupiv PCA for 24 h, n = 18 Saline via catheter, n = 18 Rescue: morphine IV/ meperidine IM PRN	Decreased only for first 4 h with activity, otherwise equivalent, p = 0.006	Decreased by 59%, p < 0.001	44% versus 100%, p = 0.003	Increased, p = 0.04	6 versus 7 d	Jadad score = 5

Nine trials and 505 patients were included in qualitative review and 7 trials with 412 patients in metaanalysis.
Bupiv, bupivacaine; LA, local anesthetic group; NA, not available; PCA, patient-controlled analgesia; PONV, postoperative nausea and vomiting; PRN, pro re nata; Ropiv, ropivacaine; VAS, visual analogue scale.

measured opioid-related side effects, but most reported a reduction in PONV (four of six RCTs), although none reached individual statistical significance. Patient satisfaction was increased considerably in the three RCTs that reported these outcomes. Length of stay was only measured in 3 RCTs, and most of the procedures (9 of 16 RCTs) were ambulatory.

Overall summary of results from quantitative and qualitative review

Continuous wound catheters consistently demonstrated analgesic efficacy in terms of reduced pain scores or opioid use for all surgical subgroups, despite heterogeneity in type of surgical procedure, location of wound catheter, mode of delivery of local anesthetic, dose of local anesthetic, and analgesic mixture. Opioid-related side effects, patient satisfaction, and length of hospital stay were infrequently assessed for each surgical group, but there was a global reduction in PONV, increased patient satisfaction, and decreased length of stay.

DISCUSSION

Uncontrolled postoperative pain can result in a number of longterm detrimental outcomes.[59] Although modalities such as epidural analgesia and continuous peripheral nerve blockade[5] can provide superior postoperative analgesia, these techniques can be limited by their initial expense (labor, equipment) and potential high failure rate (approximately 5% to 25%).[4] An alternative technique that might have widespread applicability is the insertion of catheters to allow for continuous infusions of local anesthetics into the surgical wound at the end of the procedure. We performed a quantitative and qualitative systematic review of RCTs and found that continuous wound catheters can confer several benefits, including improved analgesia, reduced opioid use and side effects, increased patient satisfaction, and reduced hospital stay.

Direct application of local anesthetic to wounds can provide analgesia through several mechanisms. Local anesthetics would directly block transmission of pain from nociceptive afferents from the wound surface. In addition, there is growing evidence that local anesthetic can inhibit local inflammatory response to injury, which can sensitize nociceptive receptors and contribute to pain and hyperalgesia. For example, studies have observed that local anesthetics reduce release of inflammatory mediators from neutrophils, reduce neutrophil adhesion to

Table 5. Randomized Controlled Trials in Orthopaedic Surgery

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Alford,[36] 2003	Anterior cruciate ligament reconstruction	Intraarticular catheter with 0.25% bupiv 2 mL/h for 4 d + femoral nerve block, n = 16 Saline via catheter, n = 12 No catheter, n = 14 Rescue: hydrocodone/ acetaminophen Ibuprofen po PRN	Decreased through POD 4, $p < 0.03$	Equivalent	NA	NA	Ambulatory surgery	Jadad score = 4
Axelsson,[37] 2003	Arthroscopic subacromial decompression	Intraarticular catheter with 0.5% ropiv PCA for 24 h, n = 20 Saline via catheter, n = 10 Rescue: morphine IV/ propoxyphene po PRN	Decreased with rest and activity for 1st 30 min, otherwise equivalent, $p < 0.05$	Decreased by 85%, $p < 0.05$	Equivalent without specifics provided	NA	Ambulatory surgery	Jadad score = 4
Barber,[55] 2002	Shoulder arthroscopy	Intraarticular catheter with 0.5% bupiv 2 mL/h for 2 d, n = 25 Saline via catheter, n = 25 Rescue: hydrocodone/ acetaminophen po PRN	Decreased through POD 7, $p < 0.05$	Decreased by 33%, $p < 0.05$	NA	NA	Ambulatory surgery	Excluded from metaanalysis as only mean values were presented Jadad score = 5
Bianconi,[38] 2003	Total hip or knee replacement	Catheter between muscle fascia and subcutaneous with 0.2% ropiv 5 mL/h for 55 h, n = 18 Saline via catheter, n = 19 Rescue: tramadol IV/diclofenac IM PRN	Decreased at rest and activity through 72 h, $p < 0.05$	Decreased by 78%, $p < 0.05$	44% versus 53%	Increased, $p < 0.01$	6.3 versus 8.8 d, $p < 0.05$	Jadad score = 3
Bianconi,[39] 2004	Spine fusion	Catheter between muscle fascia and subcutaneous with 0.2% ropiv 5 mL/h for 55 h, n = 18 Saline via catheter, n = 19 Rescue: tramadol iv/diclofenac IM PRN	Decreased at rest and activity through 72 h, $p < 0.01$	Decreased by 76%, $p < 0.05$	27% versus 37%	Increased, $p < 0.01$	5.1 versus 7.6 d, $p < 0.05$	Jadad score = 3
Blumenthal,[40] 2005	Iliac crest bone graft for shoulder surgery	Catheter next to foam over iliac crest harvest site with 0.2% ropiv 5 mL/h for 48 h, n = 18 Saline via catheter, n = 18 Rescue: morphine IV/rofecoxib/ paracetamol po PRN	Decreased at rest and activity through 48 h, $p < 0.05$	Decreased by 58%, $p < 0.05$	11% versus 17%	Increased, $p < 0.05$	Ambulatory surgery	Patient satisfaction excluded from metaanalysis due to type of data presentation Jadad score = 3

(continued)

Table 5. Continued

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Boss,[41] 2004	Open rotator cuff repair	Subacromial catheter with 0.25% bupiv 6 mL/h for 48 h, n = 20 Saline via catheter, n = 22 Rescue: IV PCA morphine	Equivalent	Equivalent	Equivalent without specifics provided	NA	NA	Jadad score = 3
Gottschalk,[42] 2003	Open shoulder surgery	Subcutaneous catheter with 0.375% ropiv 5 mL/h for 48 h, n = 15 Catheter with 0.2% ropiv, n = 12 Saline via catheter, n = 14 Rescue: piritramide IV PCA	Decreased at rest and activity through 48 h, $p < 0.005$	Decreased by 58%, $p < 0.05$	19% versus 29%	NA	NA	Jadad score = 5
Harvey,[43] 2004	Arthroscopic subacromial decompression	Intraarticular catheter with 0.2% ropiv PCA for 48 h, n = 10 Saline via catheter, n = 9 Rescue: morphine IV/ hydrocodone/acetaminophen po PRN	Decreased through POD 2, $p < 0.05$	Equivalent	NA	NA	Ambulatory surgery	Jadad score = 5
Hoenecke,[44] 2002	Anterior cruciate ligament reconstruction	Intraarticular catheter with 0.25% bupiv 2 mL/h for 48 h, n = 12 Saline via catheter, n = 14 Rescue: unspecified opioids	Decreased through 48 h, $p = 0.02$	Equivalent	NA	NA	Ambulatory surgery	Jadad score = 3
Klein,[45] 2001	Shoulder arthroscopy	Intraarticular catheter with 0.5% ropiv 2 mL/h for 48 h, n = 20 Saline via catheter, n = 20 Rescue: oxycodone/ acetaminophen po PRN	Decreased at rest and activity for POD 1 and 2, $p = 0.006$	Decreased by 19%, $p < 0.05$	NA	NA	Ambulatory surgery	Jadad score = 4
Park,[46] 2002	Shoulder arthroscopy	Intraarticular catheter with 0.5% bupiv + morphine 0.2 mg/mL 0.5 mL/h for 3 d, n = 30 Saline via catheter, n = 28 Rescue: tramadol IM PRN	Decreased at rest through POD 3, $p < 0.05$	Decreased by 88%, $p < 0.05$	NA	NA	NA	Jadad score = 3
Puri,[56] 2000	Iliac crest bone graft for anterior cervical diskectomy or foot arthrodesis	Catheter at the iliac crest harvest site with 0.5% bupiv 10 mL q 8 h for 24 h, n = 13 Saline via catheter, n = 13 Rescue: unspecified	Equivalent	Equivalent	NA	NA	NA	Excluded from metaanalysis as no data were presented Crossover design Jadad score = 4

(continued)

Table 5. Continued

First author, year	Type of operation	Analgesic regimen	Pain scores LA versus control	Opioid use LA versus control	PONV LA versus control	Patient satisfaction LA versus control	Length of stay LA versus control	Other outcomes/ comments
Quick,[47] 2003	Shoulder arthroscopy	Intraarticular catheter with 0.5% bupiv + 1:200,000 epinephrine 2 mL/h for 50 h, n = 50 Catheter placed but inactive pump, n = 50 Rescue: unspecified	Equivalent	Equivalent	8% versus 8%	NA	Ambulatory surgery	Opioid use excluded from metaanalysis as no doses were reported Jadad score = 4
Savoie,[57] 2000	Shoulder arthroscopy	Intraarticular catheter with 0.25% bupiv 2 mL/h for 48 h, n = 31 Saline via catheter, n = 31 Rescue: oxycodone/ acetaminophen po PRN	Decreased through POD 5, $p < 0.05$	Decreased by 35%, $p < 0.05$	NA	NA	Ambulatory surgery	Excluded from metaanalysis as only mean values were presented Jadad score = 2
Singh,[58] 2005	Iliac crest bone graft for spinal arthrodesis	Catheter at the iliac crest harvest site with 0.5% bupiv 2 mL/h for 48 h, n = 15 Saline via catheter, n = 22 Rescue: hydromorphone IV PCA	Equivalent	Decreased by 53%, $p = 0.025$	NA	NA	4.3 versus 3.9 d	Pain scores and opioid use excluded from metaanalysis as only mean values were presented Jadad score = 5

Sixteen trials with 683 patients were included in qualitative review and 12 trials with 562 patients in metaanalysis.
Bupiv, bupivacaine; LA, local anesthetic group; NA, not available; PCA, patient-controlled analgesia; PONV, postoperative nausea and vomiting; PRN, pro re nata; Ropiv, ropivacaine.

the endothelium, reduce formation of free oxygen radicals, and decrease edema formation.[60,61] Regardless of mechanisms, the ability to provide prolonged application of local anesthetic to wounds through a catheter was probably important, as previous systematic reviews have been unable to detect appreciable benefit from single injection of local anesthetic in abdominal operation or laparoscopy.[62,63]

Use of continuous wound catheters consistently reduced need for opioids, both as rescue and total dose. Opioid-sparing provided objective evidence for efficacy of continuous wound catheters and likely contributed to decreased incidence of PONV. With incidence ranging from 30% to 80%,[64] PONV has been consistently rated by patients as a primary concern after operation that is more important than postoperative pain.[64,65] PONV can result in major patient discomfort, poor satisfaction, and increased economic burden, as it has been identified as a major cause of increased nursing care and delayed discharge or unplanned hospital admission after ambulatory surgery.[64]

Reduction of risk of PONV with continuous wound catheters might have contributed to increased patient satisfaction, although this was an infrequently measured result in RCTs. Reduced length of hospital stay was associated with continuous wound catheters, especially in the cardiothoracic and orthopaedic surgery subgroups. Metaanalysis suggested potential saving of 1 day of hospital stay. If verified, this would represent a substantial cost savings, as typical wound catheter equipment costs range from $200 to $280 per patient.[6,18] Reasons for reduced hospital stay are unclear, as few RCTs strictly defined discharge criteria or applied clinical pathways to standardize postoperative recovery. A large number of RCTs were performed in ambulatory surgery patients, and it would be interesting to examine if continuous wound catheters could accelerate patient discharge or reduce hospital admission in this environment.

Incidences of technical failure (1%) or local anesthetic toxicity (0%) from wound catheters were low. Several reports have raised potential concern about wound infections from the presence of the catheter.[66] Reported wound infection rates were similar between active (0.7%) and control groups (1.2%). Nearly all patients in this review had an active or control catheter placed, so no comparisons with a noncatheter group can be made.

There are several limitations to our review. Although a random-effects model was used for metaanalysis because of statistical heterogeneity, the summary estimates of effect (odds ratio and weighted mean difference) should be interpreted with caution. The relative merits and agreement between metaanalyses and large RCTs are controversial. Several studies have reported varying amounts of agreement in magnitude of difference or statistical significance (65% to 90%) between meta-analyses and large RCTs, although still concluding that metaanalyses and large RCTs usually point in the same direction.[67] Future large homogenous RCTs would be valuable to verify the findings in this review and provide better quantitative data. In addition, we were not able to determine formal cost-effectiveness, optimal site for catheter placement, or optimal dosage from our systematic review because of variability in the surgical procedures for each surgery subgroup and variable placement of the catheters.

In conclusion, both quantitative and qualitative systematic review identified the efficacy of continuous wound catheters with improved analgesia, reduced opioid use and side effects, increased patient satisfaction, and, perhaps, reduced hospital stay. The most notable feature was the consistent evidence of these benefits across a wide range of surgical procedures, location of wound catheters, and dosing regimens accompanied with low incidences of catheter-related complications. Both the efficacy and technical simplicity of this technique encourage its widespread clinical use. Additional study is needed to identify ways to optimize outcomes, such as increased patient satisfaction and conversion of inpatient procedures to ambulatory procedures, with use of wound catheters.

REFERENCES

1. Wu CL, Hurley RW, Anderson GF, et al. Effect of postoperative epidural analgesia on morbidity and mortality following surgery in Medicare patients. Reg Anesth Pain Med 2004;29:525–533.
2. Apfelbaum JL, Chen C, Mehta SS, Gan TJ. Postoperative pain experience: results from a national survey suggest postoperative pain continues to be undermanaged. Anesth Analg 2003;97:534–540.
3. McGrath B, Elgendy H, Chung F, et al. Thirty percent of patients have moderate to severe pain 24 hr after ambulatory surgery: a survey of 5,703 patients. Can J Anaesth 2004;51:886–891.
4. Block BM, Liu SS, Rowlingson AJ, et al. Efficacy of postoperative epidural analgesia: a meta-analysis. JAMA 2003;290:2455–2463.
5. Richman JM, Liu SS, Courpas G, et al. Does continuous peripheral nerve block provide superior pain control to opioids? A meta-analysis. Anesth Analg 2006;102:248–257.

6. Ilfeld BM, Morey TE, Enneking FK. New portable infusion pumps: real advantages or just more of the same in a different package? Reg Anesth Pain Med 2004;29:371–376.
7. Jadad AR, Moore RA, Carroll D, et al. Assessing the quality of reports of randomized clinical trials: is blinding necessary? Control Clin Trials 1996;17:1–12.
8. Cheong WK, Seow-Choen F, Eu KW, et al. Randomized clinical trial of local bupivacaine perfusion versus parenteral morphine infusion for pain relief after laparotomy. Br J Surg 2001;88:357–359.
9. Chester JF, Ravindranath K, White BD, et al. Wound perfusion with bupivacaine: objective evidence for efficacy in postoperative pain relief. Ann R Coll Surg Engl 1989;71:394–396.
10. Fredman B, Zohar E, Tarabykin A, et al. Bupivacaine wound instillation via an electronic patient-controlled analgesia device and a double-catheter system does not decrease postoperative pain or opioid requirements after major abdominal surgery. Anesth Analg 2001;92:189–193.
11. Levack ID, Holmes JD, Robertson GS. Abdominal wound perfusion for the relief of postoperative pain. Br J Anaesth 1986; 58:615–619.
12. Pfeiffer U, Dodson ME, Van Mourik G, et al. Wound instillation for postoperative pain relief: a comparison between bupivacaine and saline in patients undergoing aortic surgery. Ann Vasc Surg 1991;5:80–84.
13. Thomas DF, Lambert WG, Williams KL. The direct perfusion of surgical wounds with local anaesthetic solution: an approach to postoperative pain? Ann R Coll Surg Engl 1983;65:226–229.
14. Barron DJ, Tolan MJ, Lea RE. A randomized controlled trial of continuous extra-pleural analgesia post-thoracotomy: efficacy and choice of local anaesthetic. Eur J Anaesthesiol 1999;16: 236–245.
15. Carabine UA, Gilliland H, Johnston JR, McGuigan J. Pain relief for thoracotomy. Comparison of morphine requirements using an extrapleural infusion of bupivacaine. Reg Anesth 1995;20: 412–417.
16. Chan VW, Chung F, Cheng DC, et al. Analgesic and pulmonary effects of continuous intercostal nerve block following thoracotomy. Can J Anaesth 1991;38:733–739.
17. Deneuville M, Bisserier A, Regnard JF, et al. Continuous intercostal analgesia with 0.5% bupivacaine after thoracotomy: a randomized study. Ann Thorac Surg 1993;55:381–385.
18. Dowling R, Thielmeier K, Ghaly A, et al. Improved pain control after cardiac surgery: results of a randomized, double-blind, clinical trial. J Thorac Cardiovasc Surg 2003;126:1271–1278.
19. Dryden CM, McMenemin I, Duthie DJ. Efficacy of continuous intercostal bupivacaine for pain relief after thoracotomy. Br J Anaesth 1993;70:508–510.
20. Francois T, Blanloeil Y, Pillet F, et al. Effect of interpleural administration of bupivacaine or lidocaine on pain and morphine requirement after esophagectomy with thoracotomy: a randomized, double-blind and controlled study. Anesth Analg 1995;80: 718–723.
21. Inderbitzi R, Flueckiger K, Ris HB. Pain relief and respiratory mechanics during continuous intrapleural bupivacaine administration after thoracotomy. Thorac Cardiovasc Surg 1992;40: 87–89.
22. Karakaya D, Baris S, Ozkan F, et al. Analgesic effects of interpleural bupivacaine with fentanyl for post-thoracotomy pain. J Cardiothorac Vasc Anesth 2004;18:461–465.
23. Raffin L, Fletcher D, Sperandio M, et al. Interpleural infusion of 2% lidocaine with 1:200,000 epinephrine for postthoracotomy analgesia. Anesth Analg 1994;79:328–334.
24. Silomon M, Claus T, Huwer H, et al. Interpleural analgesia does not influence postthoracotomy pain. Anesth Analg 2000;91: 44–50.
25. Tetik O, Islamoglu F, Ayan E, et al. Intermittent infusion of 0.25% bupivacaine through an intrapleural catheter for postthoracotomy pain relief. Ann Thorac Surg 2004;77:284–288.
26. White PF, Rawal S, Latham P, et al. Use of a continuous local anesthetic infusion for pain management after median sternotomy. Anesthesiology 2003;99:918–923.
27. Fredman B, Shapiro A, Zohar E, et al. The analgesic efficacy of patient-controlled ropivacaine instillation after Cesarean delivery. Anesth Analg 2000;91:1436–1440.
28. Givens VA, Lipscomb GH, Meyer NL. A randomized trial of postoperative wound irrigation with local anesthetic for pain after cesarean delivery. Am J Obstet Gynecol 2002;186:1188–1891.
29. Gupta A, Perniola A, Axelsson K, et al. Postoperative pain after abdominal hysterectomy: a double-blind comparison between placebo and local anesthetic infused intraperitoneally. Anesth Analg 2004;99:1173–1179.
30. Mecklem DW, Humphey MD, Hicks RW. Efficacy of bupivacaine delivered by wound catheter for post-caesarean section analgesia. Aust N Z J Obstet Gynaecol 1995;35:416–421.
31. Zohar E, Fredman B, Phillipov A, et al. The analgesic efficacy of patient-controlled bupivacaine wound instillation after total abdominal hysterectomy with bilateral salpingo-oophorectomy. Anesth Analg 2001;93:482–487.
32. Lau H, Patil NG, Lee F. Randomized clinical trial of postoperative subfascial infusion with bupivacaine following ambulatory open mesh repair of inguinal hernia. Dig Surg 2003;20:285–289.
33. Oakley MJ, Smith JS, Anderson JR, Fenton-Lee D. Randomized placebo-controlled trial of local anaesthetic infusion in day-case inguinal hernia repair. Br J Surg 1998;85:797–799.
34. Sanchez B, Waxman K, Tatevossian R, et al. Local anesthetic infusion pumps improve postoperative pain after inguinal hernia repair: a randomized trial. Am Surg 2004;70:1002–1006.
35. Schurr MJ, Gordon DB, Pellino TA, Scanlon TA. Continuous local anesthetic infusion for pain management after outpatient inguinal herniorrhaphy. Surgery 2004;136:761–769.
36. Alford JW, Fadale PD. Evaluation of postoperative bupivacaine infusion for pain management after anterior cruciate ligament reconstruction. Arthroscopy 2003;19:855–861.
37. Axelsson K, Nordenson U, Johanzon E, et al. Patient-controlled regional analgesia (PCRA) with ropivacaine after arthroscopic subacromial decompression. Acta Anaesth Scand 2003;47:993–1000.
38. Bianconi M, Ferraro L, Traina GC, et al. Pharmacokinetics and efficacy of ropivacaine continuous wound instillation after joint replacement surgery. Br J Anaesth 2003;91:830–835.
39. Bianconi M, Ferraro L, Ricci R, et al. The pharmacokinetics and efficacy of ropivacaine continuous wound instillation after spine fusion surgery. Anesth Analg 2004;98:166–172.
40. Blumenthal S, Dullenkopf A, Rentsch K, Borgeat A. Continuous infusion of ropivacaine for pain relief after iliac crest bone grafting for shoulder surgery. Anesthesiology 2005;102:392–397.
41. Boss AP, Maurer T, Seiler S, et al. Continuous subacromial bupivacaine infusion for postoperative analgesia after open acromioplasty and rotator cuff repair: preliminary results. J Shoulder Elbow Surg 2004;13:630–634.

42. Gottschalk A, Burmeister MA, Radtke P, et al. Continuous wound infiltration with ropivacaine reduces pain and analgesic requirement after shoulder surgery. Anesth Analg 2003;97: 1086–1091.
43. Harvey GP, Chelly JE, AlSamsam T, Coupe K. Patient-controlled ropivacaine analgesia after arthroscopic subacromial decompression. Arthroscopy 2004;20:451–455.
44. Hoenecke HR Jr, Pulido PA, Morris BA, Fronek J. The efficacy of continuous bupivacaine infiltration following anterior cruciate ligament reconstruction. Arthroscopy 2002;18:854–858.
45. Klein SM, Nielsen KC, Martin A, et al. Interscalene brachial plexus block with continuous intraarticular infusion of ropivacaine. Anesth Analg 2001;93:601–605.
46. Park JY, Lee GW, Kim Y, Yoo MJ. The efficacy of continuous intrabursal infusion with morphine and bupivacaine for postoperative analgesia after subacromial arthroscopy. Reg Anesth Pain Med 2002;27:145–149.
47. Quick DC, Guanche CA. Evaluation of an anesthetic pump for postoperative care after shoulder surgery. J Shoulder Elbow Surg 2003;12:618–621.
48. Baig MK, Zmora O, Derdemezi J, et al. Use of the ON-Q pain management system is associated with decreased postoperative analgesic requirement: double blind randomized placebo pilot study. J Am Coll Surg 2006;202:297–305.
49. Kushner DM, LaGalbo R, Connor JP, et al. Use of a bupivacaine continuous wound infusion system in gynecologic oncology: a randomized trial. Obstet Gynecol 2005;106:227–233.
50. Magnano D, Montalbano R, Lamarra M, et al. Ineffectiveness of local wound anesthesia to reduce postoperative pain after median sternotomy. J Card Surg 2005;20:314–318.
51. Wu CL, Partin AW, Rowlingson AJ, et al. Efficacy of continuous local anesthetic infusion for postoperative pain after radical retropubic prostatectomy. Urology 2005;66:366–370.
52. LeBlanc KA, Bellanger D, Rhynes VK, Hausmann M. Evaluation of continuous infusion of 0.5% bupivacaine by elastomeric pump for postoperative pain management after open inguinal hernia repair. J Am Coll Surg 2005;200:198–202.
53. Kristensen BB, Chistensen DS, Ostergaard M, et al. Lack of postoperative pain relief after hysterectomy using preperitoneally administered bupivacaine. Reg Anesth Pain Med 1999;24:576–580.
54. Leong WM, Lo WK, Chiu JW. Analgesic efficacy of continuous delivery of bupivacaine by an elastomeric balloon infusor after abdominal hysterectomy: a prospective randomised controlled trial. Aust N Z J Obstet Gynaecol 2002;42:515–518.
55. Barber FA, Herbert MA. The effectiveness of an anesthetic continuous-infusion device on postoperative pain control. Arthroscopy 2002;18:76–81.
56. Puri R, Moskovich R, Gusmorino P, Shott S. Bupivacaine for postoperative pain relief at the iliac crest bone graft harvest site. Am J Orthop 2000;29:443–446.
57. Savoie FH, Field LD, Jenkins RN, et al. The pain control infusion pump for postoperative pain control in shoulder surgery. Arthroscopy 2000;16:339–342.
58. Singh K, Samartzis D, Strom J, et al. A prospective, randomized, double-blind study evaluating the efficacy of postoperative continuous local anesthetic infusion at the iliac crest bone graft site after spinal arthrodesis. Spine 2005;30:2477–2483.
59. Perkins FM, Kehlet H. Chronic pain as an outcome of surgery. A review of predictive factors. Anesthesiology 2000;93:1123–1133.
60. Holman MW, Duryea ME. Local anesthetics and the inflammatory response: a new therapeutic indication? Anesthesiology 2000;93:858–875.
61. Hahnenkamp K, Theilmeier G, Van Aken HK, Hoenemann CW. The effects of local anesthetics on preoperative coagulation, inflammation, and microcirculation. Anesth Analg 2002;94: 1441–1447.
62. Moiniche S, Mikkelsen S, Wetterslev J, Dahl JB. A qualitative systematic review of incision local anesthesia for postoperative pain relief after abdominal operations. Br J Anaesth 1998;81: 377–383.
63. Moiniche S, Jorgensen H, Wetterslev J, Dahl JB. Local anesthetic infiltration for postoperative pain relief after laparoscopy: a qualitative and quantitative systematic review of intraperitoneal, port-site infiltration and mesosalpinx block. Anesth Analg 2000;90:899–912.
64. Gan TJ, Meyer T, Apfel CC, et al. Consensus guidelines for managing postoperative nausea and vomiting. Anesth Analg 2003;97:62–71.
65. Apfel CC, Korttila K, Abdalla M, et al. A factorial trial of six interventions for the prevention of postoperative nausea and vomiting. N Engl J Med 2004;350:2441–2451.
66. Brown SL, Morrison AE. Local anesthetic infusion pump systems adverse events reported to the Food and Drug Administration. Anesthesiology 2004;100:1305–1307.
67. Ioannidis JP, Cappelleri JC, Lau J. Issues in comparisons between meta-analyses and large trials. JAMA 1998;279:1089–1093.