Joshi GP,* Bonnet F, Shah R, Wilkinson RC, Camu F, Fischer B, Neugebauer EAM, Rawal N, Schug SA, Simanski C, Kehlet H. A systematic review of randomized trials evaluating regional techniques for post-thoracotomy analgesia. ***Anesthesia and Analgesia*** **2008; 107: 1026-1040.**

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Abstract

BACKGROUND: Thoracotomy induces severe postoperative pain and impairment of pulmonary function, and therefore regional analgesia has been intensively studied in this procedure. Thoracic epidural analgesia is commonly considered the "gold standard" in this setting; however, evaluation of the evidence is needed to assess the comparative benefits of alternative techniques, guide clinical practice and identify areas requiring further research.

METHODS: In this systematic review of randomized trials we evaluated thoracic epidural, paravertebral, intrathecal, intercostal, and interpleural analgesic techniques, compared to each other and to systemic opioid analgesia, in adult thoracotomy. Postoperative pain, analgesic use, and complications were analyzed.

RESULTS: Continuous paravertebral block was as effective as thoracic epidural analgesia with local anesthetic (LA) but was associated with a reduced incidence of hypotension. Paravertebral block reduced the incidence of pulmonary complications compared with systemic analgesia, whereas thoracic epidural analgesia did not. Thoracic epidural analgesia was superior to intrathecal and intercostal techniques,

although these were superior to systemic analgesia; interpleural analgesia was inadequate.

CONCLUSIONS: Either thoracic epidural analgesia with LA plus opioid or continuous paravertebral block with LA can be recommended. Where these techniques are not possible, or are contraindicated, intrathecal opioid or intercostal nerve block are recommended despite insufficient duration of analgesia, which requires the use of supplementary systemic analgesia. Quantitative meta-analyses were limited by heterogeneity in study design, and subject numbers were small. Further well designed studies are required to investigate the optimum components of the epidural solution and to rigorously evaluate the risks/benefits of continuous infusion paravertebral and intercostal techniques compared with thoracic epidural analgesia.

Appendix Tables A–S.

Table A. Thoracic epidural LA plus opioid *versus* systemic opioid analgesia

Study	Epidural LA + opioid (ELO) *vs.* systemic analgesia (S) (number of patients)	Quality score	Pain (ELO *vs.* S)					Supplementary analgesic use (ELO *vs.* S)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (ELO *vs.* S)
			Day 0	Day 1	Day 2	Day 3	Quantitative outcomes (WMD, VAS 0–100 mm)		
Administration started or continued postoperatively									
[1]Azad *et al*. 2000	Epidural infusion bupivacaine/ropivacaine + fentanyl (25) *vs*. IV PCA piritramide (25)	B1	↓ r c	↓ r c	↓ c NS r	↓ r c	**Pain scores at rest:** **12 h:**[2,3] -19.69 [-25.41, -13.96], p<0.00001. **Day 1:**[1-5] -14.50 [-21.74, -7.26], p<0.0001. **Day 2:**[1-5] -11.04 [-21.07, -1.00], p=0.03. **Day 3:**[1,2,4,5] -10.48 [-15.64, -5.32], p<0.0001. **Pain scores on coughing:** **12 h:**[2,3] -28.26 [-52.88, -3.64], p=0.02. **Day 1:**[1-3] -21.83 [-30.20, -13.46], p<0.00001. **Day 2:**[1-3] -18.79 [-23.11, -14.48], p<0.00001. **Day 3:**[1,2] -19.95 [-26.48, -13.41], p<0.00001.	No statistical analysis reported	**Quantitative outcomes** **Incidence of pulmonary complications:**[1,2,6,4] 0.92 [0.48, 1.75], p=0.79. **Incidence of hypotension**:[2,6,7,4] 3.80 [1.57, 9.23], p=0.003. **Incidence of nausea and/or vomiting**:[2-4,6] 0.79 [0.47, 1.33], p=0.38. **Incidence of pruritus**:[2-4,6] 1.60 [0.95, 2.70], p=0.08. **Qualitative outcomes** Incidence of sedation:[2,1] NS.
[2]Boisseau *et al*. 2001	Epidural infusion ropivacaine + sufentanil (25) *vs*. IV PCA morphine (25)	B3	↓ r c	↓ c NS r	↓ c NS r	↓ c NS r		–	
[8]Brichon *et al*. 1994	Epidural infusion bupivacaine + fentanyl (46) *vs*. IV buprenorphine injection (33)	B2	–	↓ r	↓ r	↓ r		Reduced IV and oral supplementary analgesia in ELO	
[6]Della Rocca *et al*. 2002	Epidural infusion bupivacaine/lidocaine + morphine (286) *vs.* IV PCA morphine (277)	B2	↓ r m	–	–	–		Reduced frequency of requests in ELO	
[7]Licker *et al*. 2003	Epidural infusion bupivacaine + fentanyl (17) *vs*. IV PCA morphine (18)	B2	VAS ≤ 30 mm in both groups, NS for 48 h			–		–	
[4]Logas *et al*. 1987	Epidural infusion bupivacaine + morphine (11) *vs.* IM morphine injection (10)	A4	NS r	↓ r	↓ r	↓ r		Reduced total morphine use in ELO	

[3]Senturk *et al*. 2002 (comparison arm 1)	Epidural bupivacaine + morphine, pre, intra- and PCEA postoperatively (22) *vs.* IV PCA morphine (23)	B2	↓ r m c	↓ r m c	↓ r m c	–		–	
[3]Senturk *et al*. 2002 (comparison arm 2)	Epidural bupivacaine + morphine, PCEA postoperatively (24) *vs.* IV PCA morphine (23)	B2	↓ r not m c	↓ r not m c	↓ r not m c	–		–	
[5]Zwarts *et al*. 1989	Epidural infusion bupivacaine + sufentanil (10) *vs.* IM nicomorphine injection (10)	B2	–	↓ r m	↓ r m	↓ r m		–	

↓ = significant benefit of thoracic epidural LA + opioid for reducing pain scores and/or frequency of pain ($p<0.05$), compared with systemic analgesia, on at least one time point on days 0 to 3 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; – = not recorded; IV = intravenous; IM = intramuscular; PCA = patient controlled analgesia; PCEA = patient controlled epidural analgesia; WMD = weighted mean difference; OR = odds ratio

Table B. Thoracic epidural LA *versus* systemic opioid analgesia

Study	Epidural LA (EL) *vs.* systemic analgesia (S) (number of patients)	Quality score	Pain (no quantitative analyses possible) (EL *vs.* S)				Supplementary analgesic use (EL *vs.* S)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (EL *vs.* S)
			Day 0	Day 1	Day 2	Day 3		
Administration started or continued postoperatively								
[9]Bachmann-Mennenga 1993	Epidural infusion bupivacaine (10) *vs.* IV buprenorphine injection (10)	B2	Reduced in EL, no p value	–	–	–	Reduced total IV buprenorphine use in EL	**Quantitative outcomes** **Incidence of pulmonary complications:**[4,10] 0.43 [0.12, 1.60], p=0.21 **Qualitative outcomes** Incidence of nausea and vomiting,[4] and pruritus:[4] NS
[4]Logas 1987	Epidural infusion bupivacaine (10) *vs.* IM morphine injection (10)	A4	NS r	NS r	NS r	NS r	NS total morphine use	
[10]Von-Dossow 2001	Epidural bupivacaine at intervals (25) *vs.* IV PCA piritramide (25)	B2	↓ r	↓ r	↓ r	NS r	–	

↓ = significant benefit of thoracic epidural LA for reducing pain scores ($p<0.05$), compared with systemic analgesia, on at least one time point on days 0 to 3 postoperatively, as indicated; r = at rest; NS = not significant; – = not recorded; IV = intravenous; IM = intramuscular; PCA = patient controlled analgesia

Table C. Thoracic epidural opioid *versus* systemic opioid

Study	Epidural opioid (EO) *vs.* systemic analgesia (S) (number of patients)	Quality score	Pain (no quantitative analyses possible) (EO *vs.* S)				Supplementary analgesic use (EO *vs.* S)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (EO *vs.* S)
			Day 0	Day 1	Day 2	Day 3		
Lipophilic opioid *Administration started or continued postoperatively*								
[11]Benzon *et al*. 1993	Epidural infusion fentanyl (18) *vs.* IV PCA morphine (18)	B5	↓ r c	↓ r c	↓ r c	↓ r c	NS volume analgesic solution used	**Quantitative outcomes** **Incidence of pulmonary complications:**[12,13] 0.84 [0.27, 2.65], p=0.77. **Incidence of nausea:**[12,13] 0.14 [0.05, 0.42], p=0.0005. **Incidence of pruritus:**[11-13] 4.22 [1.30, 13.72], p=0.02. **Qualitative outcomes** Reduced incidence of nausea and/or vomiting in EO in 2/3 studies;[12,13] NS.[11] Reduced frequency of high sedation levels in EO.[11] Incidence of urinary retention:[13] NS.
[12]Guinard *et al*. 1992	Epidural infusion fentanyl (16) *vs.* IV infusion fentanyl (16)	B3	NS r c	NS r c	NS r c	–	Reduced fentanyl use in EO	
[13]Salomaki *et al*. 1991	Epidural infusion fentanyl (20) *vs.* IV infusion fentanyl (20)	B3	NS r	NS r	–	–	Reduced fentanyl use in EO	
Hydrophilic opioid *Administration started or continued postoperatively*								
[14]Bloch *et al*. 2002	Epidural infusion morphine (30) *vs.* IV PCA morphine (30)	A5	↓ r c	NS r c	–	–	Reduced morphine use in EO	**Qualitative outcomes** Incidence of adverse effects (including nausea, vomiting, sedation, hypotension, and/or urinary retention and/or pulmonary complications): NS[4,14,15]
[16]Hasenbos *et al*. 1986	Epidural bolus nicomorphine (14) *vs.* IM injection nicomorphine (10)	B2	NS r, at time of maximal pain relief				–	

[15]Larsen *et al*. 1986	Epidural morphine at intervals (10) *vs.* SC nicomorphine injections (10)	B3	NS r	NS r	NS r	–	No statistical analysis	
[4]Logas *et al*. 1987	Epidural infusion morphine (12) *vs.* IM injection morphine (10)	A4	NS r	NS r	↓ r	↓ r	Reduced morphine use in EO	
[14]Bloch *et al*. 2002	Epidural infusion morphine (30) *vs.* IV infusion tramadol (29)	A5	NS r c	NS r c	–	–	NS morphine use	**Quantitative outcomes** **Incidence of PONV:**[14,17] OR 6.81 [0.79, 58.65], p=0.08 **Qualitative outcomes** Sedation scores: NS[14]
[17]James *et al*. 1996	Epidural infusion morphine (19) *vs.* IV injection tramadol (20)	A5	NS r	NS r	–	–	NS morphine use	

↓ = significant benefit of thoracic epidural opioid for reducing pain scores ($p<0.05$), compared with systemic analgesia, on at least one time point on days 0 to 3 postoperatively, as indicated; r = at rest; c = on coughing; NS = not significant; – = not recorded; IV = intravenous; IM = intramuscular; SC = subcutaneous; PONV = postoperative nausea and vomiting; PCA = patient controlled analgesia

Table D. Thoracic paravertebral block *versus* paravertebral saline or no paravertebral block (all patients received systemic analgesia)

Study	Paravertebral block (PV) *vs.* paravertebral saline (S) or no paravertebral block (C) (number of patients)	Quality score	Pain (PV *vs.* S or C)					Supplementary analgesic use (PV *vs.* S or C)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (PV *vs.* S or C)
			Day 0	Day 1	Day 2	Day 3 to 5	Quantitative outcomes (WMD, VAS 0–100 mm)		
Paravertebral LA *Continued postoperatively*									
[18]Barron *et al*. 1999	Paravertebral bupivacaine (21) *vs.* paravertebral lidocaine (22) *vs.* paravertebral saline (20), continued postoperatively by infusion (both groups received postoperative IV morphine infusion)	A4	NS r	↓ r	↓ r	Day 3 NS r	**Pain at rest:** **8 h:**[18-20] -14.15 [-30.55, 2.24], p=0.09. **Day 1:**[18-21]-8.68 [-14.79, -2.57], p=0.005. **Day 2:**[18-21] -10.69 [-26.08, 4.70], p=0.17. **Day 3:**[18,20,21] -14.07 [-31.93, 3.78], p=0.12. **Day 5:**[20,21] -8.45 [-30.24, 13.35], p=0.45.	Reduced total morphine use in PV	**Quantitative outcomes** **Incidence of pulmonary complications:**[18-24] 0.17 [0.09, 0.33], p<0.00001. **Qualitative outcomes:** Incidence of PONV: NS.[25]
[22]Berrisford *et al*. 1990	Paravertebral bupivacaine (25) *vs.* paravertebral saline (21), continued postoperatively by infusion (both groups received IM papaveretum by injection)	B4	↓ r	↓ r	↓ r	Days 3 and 5 ↓ r		Reduced papaveretum use in PV	
[23]Bilgin *et al*. 2003	Paravertebral bupivacaine (25) *vs.* IV metamizol injection (administered at 4 h intervals)	B1	↓ r c	↓ r c	↓ r c	Day 3 ↓ r c		–	
[25]Carabine *et al*. 1995	Paravertebral bupivacaine infusion (10) *vs.* no paravertebral infusion (10) (both groups received IV PCA morphine)	B3	↓ r m	↓ r m	–	–		Reduced morphine use in PV	
[19]Carretta *et al*. 1996	Paravertebral bupivacaine at intervals (10) *vs.* IM ketorolac injection (10) *vs.* no paravertebral block or ketorolac injection (10) (all groups received IM meperidine on demand)	B2	NS r	NS r	NS r	–		Reduced meperidine use in PV *vs.* C, but reduced meperidine use with IM ketorolac	

								vs. PV	
[21]Deneuville *et al* 1993	Paravertebral bupivacaine (23) *vs.* paravertebral saline (23) *vs.* no paravertebral block (29), continued postoperatively by infusion (all groups received IM buprenorphine by injection)	A4	**P** *vs.* **C**: ↓ r **P** *vs.* **S**: NS	**P** *vs.* **S** or **C**: NS r	**P** *vs.* **S** or **C**: NS r	Days 3 to 5 **P** *vs.* **S** or **C**: NS r		Reduced buprenorphine use in PV and S *vs.* C; NS between PV and S	
[20]Eng *et al* 1992	Paravertebral bupivacaine (40) *vs.* paravertebral saline (40), continued postoperatively by infusion (both groups received IM papaveretum by injection)	B5	↓ r	↓ r	↓ r	Days 3 to 5 ↓ r		Reduced papaveretum use in PV	
[24]Sabanathan *et al*. 1990	Paravertebral bupivacaine (29) *vs.* paravertebral saline (27), continued postoperatively by infusion (both groups received IM papaveretum by injection)	B4	↓ r	↓ r	↓ r	Days 3 to 5 ↓ r		Reduced opiate use in PV	
Preincisional									
[26]Richardson *et al*. 1994	Preincisional paravertebral bupivacaine block *vs.* no paravertebral block (8 treatment arms, each with 7 patients; all patients received postoperative paravertebral infusion bupivacaine)	B2	↓ r	↓ r	NS r	–	–	Reduced opiate use in PV	–

↓ = significant benefit of paravertebral block for reducing pain scores ($p<0.05$), compared with paravertebral saline or no paravertebral block, on at least one time point on days 0 to 5 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; – = not recorded; IV = intravenous; IM = intramuscular; PCA = patient controlled analgesia; PONV = postoperative nausea and vomiting

Table E. Intrathecal opioid *versus* no intrathecal opioid

Study	Intrathecal opioid (IT) *vs.* no intrathecal opioid (C) (number of patients)	Quality score	Pain (IT *vs.* C)					Supplementary analgesic use (IT *vs.* C)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (IT *vs.* C)
			Day 0	Day 1	Day 2	Day 3	Quantitative outcomes (WMD, VAS 0–100 mm)		
Lipophilic opioid *Preoperative administration*									
[27]Liu *et al*. 2001 (comparison arm 1)	Intrathecal sufentanil (10) *vs.* no intrathecal opioid (19) (both groups received IV PCA morphine)	B5	↓ r c	NS r c	–	–		Reduced morphine use in IT	**Qualitative outcomes** Incidence of nausea, pruritus and urinary retention: NS[27] Degree of sedation: NS [27]
Postoperative administration									
[28]Sudarshan *et al*. 1995	Intrathecal fentanyl (10) *vs.* intrathecal saline (10) *vs*. no intrathecal treatment (10) (both groups received IV PCA morphine)	B4	↓ r c m	–	–	–		Reduced morphine use in IT	**Qualitative outcomes** Incidence of pruritus, urinary retention: NS[28]
Hydrophilic opioid *Preoperative administration*									
[27]Liu *et al*. 2001 (comparison arm 2)	Intrathecal morphine (10) *vs.* no intrathecal opioid (19) (both groups received IV PCA morphine)	B5	↓ r c	NS r c	–	–		Reduced morphine use in IT	**Qualitative outcomes** Incidence of PONV: NS[27]
Lipophilic + hydrophilic opioid *Preoperative administration*									
[27]Liu *et al*. 2001 (comparison	Intrathecal sufentanil + morphine (10) *vs.* no intrathecal opioid (19)	B5	↓ r c	NS r c	–	–	**Pain at rest:** **2 h:**[27,29] -37.55 [-63.56, -11.54],	Reduced morphine use in IT[27,29]	**Quantitative outcomes** **Incidence of urinary retention:**[27,29]

arm 3)	(both groups received IV PCA morphine)						p=0.005. **4 h:**[27,29] -21.12 [-29.44, -12.80], p<0.00001. **6 h:**[27,29] -12.47 [-20.43, -4.51], p=0.002. **12 h:**[27,29] -17.38 [-25.88, -8.87], p<0.0001. **24 h:**[27,29] -9.44 [-21.36, 2.47], p=0.12. **Pain on coughing:** **4 h:**[27,29] –39.14 [-55.84, -22.45], p<0.00001. **12 h:**[27,29] -24.13 [-35.08, -13.17], p<0.0001. **24 h:**[27,29] -20.80 [-47.30, 5.70], p=0.12.	**Quantitative analyses (WMD, mg)** Dose of titrated morphine in recovery:[27,29] -7.38 mg [-14.89, 0.13], p=0.05 Morphine use during 0–24 h:[27,29] -29.40 mg [-64.66, 5.86], p=0.1	2.39 [0.79, 7.29], p=0.12. **Qualitative outcomes** Incidence of nausea and/or vomiting: NS.[27,29] Incidence of pruritus: NS.[27] Degree of sedation: NS.[27]
[29]Mason *et al*. 2001	Intrathecal sufentanil + morphine (15) *vs*. no intrathecal opioid (15) (both groups received IV PCA morphine)	B3	↓ r c m	↓ r c m	NS r c m	NS r c m			

↓ = significant benefit of intrathecal opioid for reducing pain scores (p<0.05), compared with no intrathecal opioid, on at least one time point on days 0 to 3 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; – = not recorded; IV = intravenous; PCA = patient controlled analgesia; PONV = postoperative nausea and vomiting

Table F Intercostal nerve block *versus* no intercostal nerve block

Study	Intercostal nerve block (INB) *vs.* saline or no intercostal nerve block (C) (number of patients)	Quality score	Pain (INB *vs.* C)					Supplementary analgesic use (INB *vs.* C)	Complications and adverse effects: qualitative outcomes (INB *vs.* C)
			Day 0	Day 1	Day 2	Day 3 to 5	Quantitative outcomes (WMD, VAS 0–100 mm)		
Single dose intercostal nerve block *Intraoperative*									
[30]Kaplan *et al*. 1975	Intercostal bupivacaine + dextran (6) *vs.* intercostal saline + dextran (6) (all patients received postoperative IM morphine as needed)	B3	–	↓ (overall scores include pain, ability to cough and move)	↓ (no p value)	Day 3 ↓ (no p value	**Pain scores at rest:** **Day 1:**[31-33] -15.16 [-23.62, -6.70], p=0.0004. **Day 2:**[31-33] -13.85 [-20.91, -6.80], p=0.0001. **Day 3:**[31-33] 2.67 [-17.04, 22.38], p=0.79.	NS total morphine use	Incidence of pulmonary complications (mild pulmonary atelectasis): NS.[30,33] Incidence of hypotension: NS.[30] Incidence of sedation: NS.[31]
[31]Liu *et al.* 1995	Intercostal bupivacaine (9) *vs.* intercostal saline (11) before wound closure (all patients received intrathecal morphine before incision and IV morphine postoperatively, by injection then PCA)	B4	↓ r c	NS r c	NS r c	NS r c		NS opioid use	
[32]Takamori *et al*. 2002	Intercostal bupivacaine (20) *vs.* no intercostal bupivacaine (20) (all patients received epidural analgesia perioperatively)	B3	↓ r	↓ r	↓ r	Day 3 ↓ r (NS Days 4 and 5)		NS diclofenac use	
[33]Woltering *et al.* 1980	Intercostal bupivacaine (8) *vs.* no intercostal bupivacaine (12) (all	B3	–	NS r	NS r	Day 3 NS r		NS morphine use	

	patients received IV morphine on demand postoperatively)								
Repeat intercostal nerve blocks *Intra-/postoperative*									
[34]Chan 1991	Intercostal bupivacaine (10) *vs.* intercostal saline (10) (4 doses administered at 6-hourly intervals for 24 h; all patients received IV morphine on demand postoperatively)	B4	↓ r 1h after the second, third and fourth injections		–	–		Reduced morphine use in INB	
[9]Bachmann-Mennenga, 1993	Intercostal bupivacaine, 3 injections (10), *vs.* no intercostal bupivacaine (10) (patients received IV buprenorphine for analgesia if necessary)	B2	↓ r but no statistics available (time-points 30, 60, 120 and 240 mins post-analgesia)	–	–	–		Reduced buprenorphine use in INB	
[33]Woltering, 1980	Intercostal bupivacaine intraoperatively and postoperatively every 6 h (10) *vs.* no intercostal nerve block (12) (all patients received IV morphine every 2 h on demand postoperatively)	B3	–	NS r	NS r	Day 3 NS r		NS morphine use	
Continuous infusion intercostal nerve block *Postoperative*									
[35]Dryden 1993	Continuous infusion intercostal bupivacaine for first 24 h and saline for 2nd 24 h (10) *vs.* saline for first 24 h and	B5	↓ r over 48 h study period					Reduced morphine use in INB	Sedation and nausea scores: NS.[35]

	bupivacaine for 2nd 24 h postoperatively (10) (all patients received IV morphine postoperatively, by injection then PCA)					

↓ = significant benefit of intercostal nerve block for reducing pain scores ($p<0.05$), compared with intercostal saline or no intercostal nerve block, on at least one time point on days 0 to 5 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; – = not recorded; IV = intravenous; IM = intramuscular; PCA = patient controlled analgesia

Table G Interpleural LA *versus* systemic analgesia

Study	Interpleural LA (IP) *vs.* interpleural saline or no interpleural analgesia (C) (number of patients)	Quality score	Pain (IP *vs.* C)				Quantitative outcomes (WMD, VAS 0–100 mm) (IP *vs.* C)	Supplementary analgesic use (IP *vs.* C)	Complications and adverse effects: quantitative outcomes (OR) (IP *vs.* C)
			Day 0	**Day 1**	**Day 2**	**Day 3 to 5**			
Interpleural LA vs. systemic analgesia *Postoperative*									
[36]Broome, 1993	Interpleural bupivacaine (10) *vs.* no interpleural bupivacaine (10), administered after extubation (all patients received IV PCA morphine)	B4	↓ r 0–2 h, NS 3–6 h	–	–	–	**Pain scores at rest:** **30 min:**[36-39] -7.15 [-19.76, 5.46], p=0.27. **1 h:**[36,37,40] -15.66 [-37.56, 6.24], p=0.16. **2 h:**[36,37,40] -13.87 [-32.18, 4.44], p=0.14. **3 h:**[36,37,40] -8.94 [-19.98, 2.10], p=0.11. **6 h:**[36,37,40] 8.54 [-4.73, 21.80], p=0.21. **24 h:**[38,40-42] 8.44 [-5.40, 22.28], p=0.23. **Day 2:**[40-42] -0.83 [-10.70, 9.04], p=0.87.	Reduced morphine use in IP	**Quantitative outcomes** **Incidence of atelectasis or pneumonia**:[37,39,42] 0.28 [0.11, 0.74], p=0.01.
[43]Mann, 1992	Interpleural bupivacaine (20) *vs.* interpleural saline (20), administered after surgery and every 4 h until 48 or 72 h (all patients received IM papaveretum every 4 h as necessary)	A4	↓ r	↓ r	NS r	Day 3 ↓ r		Reduced mean total dose of papaveretum in IP. NS mean number of doses of papaveretum	
[40]Raffin, 1994	Interpleural lidocaine (8) *vs.* placebo (8), in operating room at end of surgery, bolus followed by continuous infusion (all patients received IV PCA morphine)	B4	↓ r (on arrival in ICU), NS 1–24 h	NS r	–	–		Reduced hourly morphine consumption in IP from 5–48 h (NS 0–4 h)	

[44]Symreng, 1989	Interpleural bupivacaine (7) *vs.* interpleural saline (8), 8 and 16 h after induction (all patients received IV morphine postoperatively as needed)	B4	↓ r after each injection		–	–		Increased duration of analgesia in IP	
[37]Tetik, 2004	Interpleural bupivacaine (20) *vs.* interpleural saline (20), following chest closure (all patients received IM diclofenac postoperatively as needed)	B4	↓ r at 4 h. NS 0–3 or 5–7 h	–	–	–		Reduced diclofenac use in IP. Increased duration of analgesia in IP	
[9]Bachmann-Mennenga, 1993	Interpleural bupivacaine, (10), *vs.* no interpleural bupivacaine (10) (all patients received IV buprenorphine for analgesia if necessary)	B2	↑ r, but no statistics available (time-points 30, 60, 120 and 240 mins post-analgesia)	–	–	–		Increased buprenorphine use in IP	
[41]Miguel, 1993	Interpleural bupivacaine (10) *vs.* IV morphine (11), postoperatively (all patients received IV morphine postoperatively as needed)	B2	NS r	NS r	NS r	Day 5 NS r		NS morphine use	
[38]Scheinin, 1989	Interpleural bupivacaine (10) *vs.* no interpleural bupivacaine (10) (all patients received IM oxycodone postoperatively as needed)	B1	NS r	NS r	–	–		Reduced oxycodone use in IP on day of surgery. NS doses of oxycodone required during 48 h postop	

[42]Schneider, 1993	Interpleural bupivacaine (9) *vs.* interpleural saline (10), every 4 h for 12 doses postoperatively (all patients received narcotic analgesia with morphine or meperidine on request)	A4	–	NS r	NS r	–		NS use of morphine or meperidine	
[39]Silomon, 2000	Interpleural bupivacaine (40) *vs.* interpleural saline (43) every 4 h from arrival in ICU for 10 doses (all patients received IV PCA piritramide)	B4	NS r c	–	–	–		NS piritramide consumption	

↓ = significant benefit of interpleural LA for reducing pain scores ($p<0.05$), compared with interpleural saline or no interpleural LA, on at least one time point on days 0 to 5 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; – = not recorded; IV = intravenous; IM = intramuscular; PCA = patient controlled analgesia; ICU = intensive care unit

Table H Interpleural morphine *versus* intravenous morphine

Study	Interpleural morphine (IP) *vs.* intravenous morphine (IV) (number of patients)	Quality score	Pain (IP *vs.* IV)				Supplementary analgesic use (IP *vs.* IV)
			Day 0	Day 1	Day 2	Day7	
Intraoperative							
[45]Aykac 1995	Interpleural morphine (14) *vs.* IV morphine (14), approximately 30 min before end of operation (patients did not receive supplemental analgesia)	B3	↓ r	↓ r	–	–	–
Postoperative							
[46]Welte 1992	Interpleural morphine (7) *vs.* interpleural saline (10), administered before extubation and infusions started in PACU for 24 h (all patients received IV morphine on request)	B4	NS r	NS r	–	NS r Day 7	NS morphine consumption

↓ = significant benefit of interpleural morphine for reducing pain scores ($p<0.05$) on at least one time point on days 0 to 7 postoperatively, as indicated, compared with intravenous morphine; r = at rest; NS = not significant; – = not recorded; IV = intravenous; PACU = post-anesthesia care unit

Table I Paravertebral block *versus* thoracic epidural analgesia

Study	Paravertebral block (PVB) *vs.* thoracic epidural analgesia (TEA) (number of patients)	Quality score	Pain (PVB *vs.* TEA)				Supplementary analgesic use (PVB *vs.* TEA)	Adverse effects and pulmonary complications: quantitative outcomes (OR) and qualitative outcomes (PVB *vs.* TEA)
			Day 0	Day 1	Day 2	Day 3 to 5		
Paravertebral LA *versus* ***thoracic epidural LA*** *Intra-/postoperative*								
[47]Dhole, 2001	Paravertebral bupivacaine (20) *vs.* thoracic epidural bupivacaine (21), intraoperative bolus followed by postoperative infusion (all patients received IM ketorolac postoperatively on demand)	B3	NS r c	–	–	–	NS rescue ketorolac	**Quantitative outcomes** **Incidence of hypotension:**[47-49] 0.07 [0.01, 0.40], p=0.003. **Incidence of nausea:**[49,50] 0.26 [0.09, 0.77], p=0.01. **Incidence of vomiting:**[49,50] 0.46 [0.13, 1.72], p=0.25. **Incidence of urinary retention:**[48,49] 0.28 [0.10, 0.78], p=0.01. **Qualitative outcomes** Reduced incidence of chest infection in PVB.[49] Reduced incidence of persistent chest pain at 6 months in PVB.[49]
[48]Matthews, 1989	Paravertebral bupivacaine (9) *vs.* thoracic epidural bupivacaine (10) postoperative infusion	B2	NS r	NS r	–	–	Not reported	
[50]Perttunen, 1995	Paravertebral bupivacaine (15) *vs.* thoracic epidural bupivacaine (15), administered intraoperatively, then continuous infusion postoperatively (all patients received IV PCA morphine postoperatively)	B2	NS r c	NS r c	NS r c	–	NS morphine consumption	
[51]Wedad, 2004	Paravertebral bupivacaine (20) *vs.* thoracic epidural bupivacaine (20), administered intraoperatively, then continuous infusion postoperatively (all patients received postoperative	B2	–	NS r	NS r	–	NS meperidine consumption	

	meperidine as needed)							
[49]Richardson, 1999	Paravertebral bupivacaine (49) *vs.* thoracic epidural bupivacaine (46), administered intraoperatively, then continuous infusion postoperatively (all patients received IV PCA morphine as needed)	B3	PVB ↓ r c			–	Reduced morphine consumption in PVB	
Paravertebral LA* versus *thoracic epidural LA plus opioid *Intra-/postoperative*								
[52]Kaiser 1998	Paravertebral bupivacaine (15) *vs.* thoracic epidural bupivacaine + fentanyl (15), administered intraoperatively, then continuous infusion postoperatively (patients received SC nicomorphine postoperatively on demand)	B2	NS r	NS r	PVB ↓ r	Day 3 PVB ↓ r, NS on Days 4 and 5	Reduced nicomorphine use in PVB on Day 2, but NS on Days 0, 1, 3, 4 and 5	–
[53]De Cosmo 2002	Paravertebral ropivacaine (25) *vs.* epidural ropivacaine + sufentanil (25), bolus intraoperatively then postoperative infusion (patients received ketorolac postoperatively as needed)	B3	PVB ↑ r m at 1, 4 and 8 h, NS at 12 h	NS r m	NS r m	–	NS ketorolac use	
Paravertebral LA plus opioid* versus *thoracic epidural LA plus opioid *Postoperative*								
[54]Bimston 1999	Paravertebral bupivacaine + fentanyl (30) *vs.* thoracic epidural bupivacaine + fentanyl (20), infused postoperatively (patients received 'additional analgesics' on request)	B3	PVB ↑ r	PVB ↑ r	NS r	Days 3 and 4 NS r	NS additional analgesic use	–

↓ = significant benefit of paravertebral block for reducing pain scores ($p<0.05$), compared with thoracic epidural analgesia, on at least one time point on days 0 to 5 postoperatively, as indicated; ↑ = significant increase in pain scores associated with paravertebral block compared with epidural analgesia ($p<0.05$) on at least one time point on days 0 to 5 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; – = not recorded; IV = intravenous; IM = intramuscular; SC = subcutaneous; PCA = patient controlled analgesia

Table J Paravertebral LA *versus* intercostal nerve block

Study	Paravertebral LA (PVB) *vs.* intercostal nerve block (INB) (number of patients)	Quality score	Pain (PVB *vs.* INB)			Supplementary analgesic use (PVB *vs.* INB)	Complications and adverse effects: qualitative outcomes (PVB *vs.* INB)
			Day 0	Day 1	Day 2		
Intra-/postoperative							
[50]Perttunen 1995	Paravertebral bupivacaine (15), administered intraoperatively, then continuous infusion postoperatively, *vs.* intercostal nerve block with bupivacaine (15) intraoperatively (all patients received IV PCA morphine postoperatively)	B2	NS r c	NS r c	NS r c	NS morphine consumption	Incidence of nausea and vomiting: NS.[50]

r = at rest; c = on coughing; NS = not significant; IV = intravenous; PCA = patient controlled analgesia

Table K Intrathecal opioid *versus* thoracic epidural LA plus opioid

Study	**Intrathecal opioid (SM) *vs.* thoracic epidural LA plus opioid (EBF) (number of patients)**	**Quality score**	**Pain (SM *vs.* EBF)**	**Supplementary analgesic use (SM *vs.* EBF)**	**Complications and adverse effects: qualitative outcomes (SM *vs.* EBF)**
			Days 1–2		
Perioperative					
[55]McCrory, 2002	Intrathecal morphine (10) *vs.* epidural bupivacaine + fentanyl (5), pre- and intraoperatively, then continued and titrated postoperatively (patients received rescue morphine as necessary)	B2	Combined results reported over Days 1 and 2. NS r c	No statistical analyses reported	Incidence of nausea and vomiting: NS.[55]

NS = not significant; r = at rest; c = on coughing

Table L Intercostal nerve block *versus* thoracic epidural analgesia with LA or opioid

Study	Intercostal nerve block (INB) *vs.* perioperative thoracic epidural LA (ELA) or thoracic epidural opioid (EO) (number of patients)	Quality score	Pain (INB *vs.* ELA)				Quantitative outcomes (WMD, VAS 0–100 mm) (INB *vs.* ELA)	Supplementary analgesic use (INB *vs.* ELA or ELO)	Complications and adverse effects: qualitative outcomes (INB *vs.* ELA)
			Day 0	Day 1	Day 2	Day 3 to 6			
Single intraoperative intercostal nerve block									
[56]Scheinin, 1987	Intercostal bupivacaine (10) *vs.* thoracic epidural morphine administered continuously pre- to postoperatively (8) *vs.* thoracic epidural bupivacaine administered continuously pre- to postoperatively (10) (all patients received postoperative IM oxycodone as requested)	B1	NS r	NS r	–	–	**Pain scores at rest:** **1 h**:[56,57] -4.22 [-16.79, 8.35], p=0.51. **3 h**:[56,57] -1.00 [-15.36, 13.36], p=0.89. **24 h**:[56,57] 14.80 [-0.43, 30.02], p=0.06.	Increased morphine consumption in INB *vs.* EO and ELA	Adverse events, including nausea, vomiting and pruritus: NS.[50]
[57]Asantila, 1986	Intercostal bupivacaine (10) *vs.* thoracic epidural bupivacaine preoperatively followed by postoperative infusion (10) *vs.* epidural morphine 4 mg preoperatively and on 1st postoperative morning (10) (patients received postoperative IM oxycodone as requested)	B1	NS r	NS r	–	–		Increased morphine consumption in INB *vs.* EO and ELA	
[58]Wurnig, 2002	Intercostal levobupivacaine (15) *vs.* thoracic epidural bupivacaine by continuous infusion, administered pre-, intra- and postoperatively (15) (all patients received postoperative SC nicomorphine on request)	B2	NS r c	INB ↑ r NS c	INB ↑ r NS c	Day 3 INB ↑ r, NS r on Days 4–6 NS c		Increased nicomorphine consumption in INB (no statistical analyses)	
[50]Perttunen,	Intercostal bupivacaine (15) *vs.*	B2	INB ↓ c	NS r c	NS r c	–		NS morphine	

1995	thoracic epidural bupivacaine intraoperative bolus and postoperative continuous infusion (15) (all patients had access to PCA IV morphine as needed)		NS r					consumption	
Repeat intercostal nerve blocks									
[57]Asantila, 1986	Repeated intercostal block with bupivacaine, prior to surgery, repeated after 6 h and on postoperative morning (10) *vs.* epidural bupivacaine with bupivacaine preoperatively, followed by postoperative infusion (10) *vs.* epidural morphine 4 mg injected preoperatively and on 1st postoperative morning (10) (all patients received postoperative IM oxycodone as requested)	B1	NS r	NS r	–	–	**Pain scores at rest:** **1 h**:[56,57] -3.76 [-15.99, 8.47], p=0.55. **3 h**:[56,57] -4.54 [-17.79, 8.71], p=0.50. **24 h**:[56,57] 5.93 [-10.09, 21.95], p=0.47.	No statistical analyses reported	–
[9]Bachmann-Mennenga, 1993	Intercostal nerve block with bupivacaine, 3 postoperative injections (10) *vs.* thoracic epidural bupivacaine, bolus injection postoperatively followed by continuous infusion (10) (all patients received IV buprenorphine postoperatively if needed)	B2	NS r	–	–	–		NS buprenorphine consumption	–
[56]Scheinin, 1987	Repeated intercostal block with bupivacaine after induction, before surgery and postoperatively (11) *vs.* thoracic epidural morphine administered continuously pre-	B1	NS r	NS r	–	–		NS morphine consumption	–

	to postoperatively (8) *vs.* thoracic epidural bupivacaine administered continuously pre- to postoperatively (10) (all patients received postoperative IM oxycodone as requested)								
Continuous infusion intercostal nerve block									
[59]Debreceni, 2003	Continuous infusion intercostal bupivacaine (22) *vs.* thoracic epidural bupivacaine infusion postoperatively (25) (all patients were given IV fentanyl if analgesia was not satisfactory)	B4	INB ↑ r at 4, 8 and 12 h, NS at 16 and 20 h	–	–		NS fentanyl use	–	

↓ = significant benefit of intercostal nerve block for reducing pain scores ($p<0.05$), compared with epidural analgesia, on at least one time point on days 0 to 6 postoperatively, as indicated; ↑ = significant increase in pain scores associated with intercostal nerve block compared with epidural analgesia ($p<0.05$) on at least one time point on days 0 to 6 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; IV = intravenous; IM = intramuscular; PCA = patient controlled analgesia; – = not recorded

Table M Interpleural LA *versus* epidural analgesia

Study	Interpleural LA (IP) *vs.* epidural analgesia (EA) (number of patients)	Quality score	Pain (IP *vs.* EA)				Supplementary analgesic use (IP *vs.* EA)	Complications and adverse effects: qualitative outcomes (IP *vs.* EA)
			Day 0	Day 1	Day 2	Day 5		
Interpleural LA* versus *thoracic epidural analgesia								
[9]Bachmann-Mennenga, 1993	Interpleural bupivacaine, bolus dose followed by continuous infusion postoperatively (10) *vs.* thoracic epidural bupivacaine, bolus injection postoperatively followed by continuous infusion (10) (all patients received IV buprenorphine postoperatively if needed)	B2	IP ↑ r, but no statistical analyses	–	–	–	Increased buprenorphine use in IP	Incidence of pneumonia: NS.[60]
[60]Brockmeier, 1994	Interpleural bupivacaine, bolus and continuous infusion postoperatively (16) *vs.* thoracic epidural bupivacaine, bolus then continuous infusion postoperatively (16) (all patients received IV morphine postoperatively as required)	B4	NS r c	–	–	–	NS morphine use	
Interpleural LA plus wound infiltration* versus *thoracic epidural LA								
[51]Wedad, 2004	Interpleural bupivacaine (bolus followed by continuous infusion) plus wound infiltration (immediately after skin closure) with bupivacaine (20) *vs.* thoracic epidural bupivacaine, bolus before wound closure and continuous infusion in recovery (20) (all patients received meperidine	B2	–	NS r	IP ↑ r	–	Increased meperidine use in IP + wound infiltration	

	on demand)							

↑ = significant increase in pain scores associated with interpleural nerve block ($p<0.05$), compared with epidural analgesia, on at least one time point on days 0 to 5 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; IV = intravenous; IM = intramuscular; PCA = patient controlled analgesia; – = not recorded; ICU = intensive care unit

Table N Interpleural analgesia *versus* thoracic paravertebral LA

Study	Interpleural analgesia (IP) *vs.* paravertebral LA (PVB) (number of patients)	Quality score	Pain (PVB *vs.* IP)			Supplementary analgesic use (IP *vs.* PVB)	Complications and adverse effects: qualitative outcomes (IP *vs.* PVB)
			Day 0	Day 1	Day 2		
Perioperative							
[61]Richardson 1995	Interpleural bupivacaine (23) *vs.* paravertebral bupivacaine (22) pre- and intraoperative injections, then postoperative infusion (all patients had access to IV PCA morphine on demand)	B3	NS r	NS r	NS r	NS morphine consumption	Increased frequency of respiratory morbidity in IP (no statistical analyses).[61]
[62]Richardson 1998	Interpleural bupivacaine (6) *vs.* paravertebral bupivacaine (5); pre- and intraoperative injections, then postoperative infusion (all patients had access to IV PCA morphine on demand)	B5	NS r	NS r	NS r	NS morphine consumption	
[51]Wedad 2004	Interpleural bupivacaine (plus wound infiltration with bupivacaine) (20) *vs.* paravertebral bupivacaine (20), administered intraoperatively, then continuous infusion postoperatively (all patients received postoperative meperidine as needed)	B2	–	NS r	IP ↑ r	Increased total meperidine consumption in IP	

↑ = significant increase in pain scores associated with interpleural analgesia compared with paravertebral block ($p<0.05$) at various time points measured on days 0 to 5 postoperatively, as indicated; r = at rest; NS = not significant; IV = intravenous; PCA = patient controlled analgesia; – = not recorded

Table O Interpleural LA *versus* intercostal nerve block

Study	Interpleural LA (IP) *vs.* intercostal nerve block (INB) (number of patients)	Quality score	Pain (IP *vs.* INB)			Supplementary analgesic use (IP *vs.* INB)
			Day 0	Day 1	Day 2	
[9]Bachmann-Mennenga, 1993	Interpleural bupivacaine, bolus followed by continuous infusion postoperatively (10) *vs.* intercostal nerve block with bupivacaine, 3 injections (10) (all patients received IV buprenorphine postoperatively if needed)	B2	IP ↑ r, but no stats	–	–	Increased buprenorphine use in IP
[63]Shafei, 1990	Interpleural bupivacaine, maximum 6 injections daily postoperatively (16) *vs.* intercostal nerve block with bupivacaine (16) (all patients received papaveretum in the first 2 days postoperatively if needed, and buprenorphine, dextropropoxyphine and paracetamol from day 3 onwards)	B3	NS r (VAS recorded every 4 h for 48 h, but reported as average VAS score)			Reduced papaveretum use and number of requests for oral analgesics in IP

↑ = significant increase in pain scores associated with interpleural nerve block compared with intercostal nerve block ($p<0.05$) on at least one time point on days 0 to 2 postoperatively, as indicated; r = at rest; NS = not significant; IV = intravenous; – = not recorded

Table P Thoracic epidural LA plus lipophilic opioid *versus* thoracic epidural lipophilic opioid alone

Study	Thoracic epidural LA plus lipophilic opioid (LAO) *vs.* thoracic epidural lipophilic opioid alone (O) (number of patients)	Quality score	Pain (LAO *vs.* O)			Supplementary analgesic use (LAO *vs.* O)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (LAO *vs.* O)
			Day 0	Day 1	Day 2		
[64]George, 1991	Thoracic epidural bupivacaine + fentanyl (10) *vs.* thoracic epidural saline + fentanyl (11), postoperative injection then continuous infusion (if additional analgesia requested by patient, IV morphine was administered)	B4	LA ↓ r	NS r	NS r	NS morphine use and test solution used	**Quantitative outcomes** **Incidence of nausea:** [16,65,66] 0.98 [0.48, 1.99], p=0.95. **Incidence of vomiting:** [16,65] 1.36 [0.37, 5.02], p=0.65. **Incidence of pruritus:** [16,64-66] 1.15 [0.52, 2.53], p=0.73. **Incidence of hypotension:** [96,67] 3.34 [0.90, 12.44], p=0.07. **Qualitative outcomes** Sedation scores lower in LA;[65] incidence of sedation: NS.[67] Incidence of nausea or emetic symptoms: NS.[64,67] Incidence of pruritus: NS.[67] Incidence of urinary retention: NS.[64]
[65]Hansdottir, 1996	Thoracic epidural sufentanil + bupivacaine (14) *vs.* thoracic epidural sufentanil infusion (12), continuous perioperative infusion (all patients received IV ketorolac or rectal diclofenac for postoperative analgesia if needed)	B4	LA ↓ m NS r	LA ↓ m NS r	LA ↓ m NS r	Reduced NSAID use in LAO	
[67]Liu, 1995	Thoracic epidural bupivacaine 0.1% + fentanyl (6; group LA0.1) *vs.* bupivacaine 0.05% + fentanyl (6; group LA0.05) *vs.* bupivacaine 0.01% + fentanyl (6; group LA0.01) *vs.* fentanyl alone (6), intraoperative infusion continued postoperatively (all patients received PCEA/epidural fentanyl as required)	B4	NS r c m	LA 0.05 and LA 0.1 ↓ m NS r c	LA 0.05 and LA 0.1 ↓ m NS r c	Reduced fentanyl consumption on POD 1 in LA0.05 and LA0.1; Reduced fentanyl consumption on POD 2 in LA0.01, LA0.05 and LA0.1 (p<0.03)	
[66]Mahon,	Thoracic epidural bupivacaine	A4	LA1 and	NS r c (at 24	–	NS volume of epidural	

1999	0.1% + fentanyl (30; group LA1) *vs.* bupivacaine 0.2% + fentanyl (32; group LA2) *vs.* fentanyl alone (33), intraoperative bolus then continuous infusion (if analgesia was insufficient, bolus of solution was given or infusion rate increased)		LA2 ↓ c NS r	h)		solution administered	
[68]Burgess, 1994	Thoracic epidural infusion fentanyl + bupivacaine 0.03% (10) *vs.* fentanyl + bupivacaine 0.06% (10) *vs.* fentanyl + bupivacaine 0.125% (10) *vs.* fentanyl alone (10), after induction, continuing postoperatively (supplemental epidural fentanyl was given if necessary)	A5	NS r	NS r	–	Increased fentanyl use in O compared with all other groups	

↓ = significant benefit of epidural LA + opioid for reducing pain scores ($p<0.05$), compared with epidural opioid alone, on at least one time point on days 0 to 5 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; IV = intravenous; PCEA = patient controlled epidural analgesia; – = not recorded

Table Q Thoracic epidural LA plus hydrophilic opioid *versus* thoracic epidural hydrophilic opioid alone

Study	Thoracic epidural LA plus hydrophilic opioid (LAO) *vs.* thoracic epidural hydrophilic opioid alone (O) (number of patients)	Quality score	Pain (LAO *vs.* O)				Supplementary analgesic use (LAO *vs.* O)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (LAO *vs.* O)
			Day 0	Day 1	Day 2	Day 3		
[69]Singh 1997	Epidural bupivacaine with hydromorphone (20) *vs.* epidural hydromorphone (23), preoperative bolus and postoperative PCEA	B4	LA ↓ c m NS r	LA ↓ c NS r m	–	–	NS hydromorphone requirement Reduced number of patients requiring treatment for breakthrough pain in LAO ($p<0.05$)	**Quantitative outcomes** **Incidence of nausea and vomiting:**[23,70] 1.63 [0.59, 4.53], p=0.35. **Incidence of pruritus:** [23,70] 0.41 [0.06, 2.93], p=0.38. **Incidence of hypotension:** [23,70] 2.92 [0.84, 10.17], p=0.09. **Qualitative outcomes** Incidence of pruritus, nausea/vomiting and hypotension: NS.[4,69] More patients withdrawn from study due to adverse effects with LA0.1.[70]
[70]Etches, 1996	Epidural bupivacaine 0.01% + meperidine (21; group LA0.01) *vs.* epidural bupivacaine 0.1% + meperidine (23; group LA0.1) *vs.* epidural meperidine (22; group O), bolus intraoperatively then infusion until PACU, (patients had access to study drug *via* PCEA as needed)	B4	NS r c	NS r c	NS r c	NS r c	NS meperidine consumption	
[4]Logas, 1987	Epidural bupivacaine + morphine (11) *vs.* epidural morphine (12), infusion started after induction and continued postoperatively (infusion rate increased postoperatively or IM morphine administered if analgesia inadequate)	A4	NS r	NS r	NS r	NS r	NS supplemental morphine use or total supplemental + epidural analgesic use	

↓ = significant benefit of epidural LA + opioid for reducing pain scores ($p<0.05$), compared with epidural opioid alone, on at least one time point on days 0 to 5 postoperatively, as indicated; r = at rest; m = on movement; c = on coughing; NS = not significant; IV = intravenous; IM = intramuscular; PCEA = patient controlled epidural analgesia; PACU = post-anesthesia care unit; – = not recorded

Table R Thoracic epidural opioid plus LA *versus* thoracic epidural LA, with or without systemic opioid

Study	Thoracic epidural opioid plus LA (LAO) *vs.* thoracic epidural LA with or without systemic opioid (LA) (number of patients)	Quality score	Pain (LAO *vs.* LA)				Supplementary analgesic use (LAO *vs.* LA)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (LAO *vs.* LA)
			Day 0	Day 1	Day 2	Day 3		
Thoracic epidural opioid plus LA* versus *thoracic epidural LA alone								
[71]Macias, 2002	Epidural ropivacaine + fentanyl (25; group RLAO) *vs.* epidural bupivacaine + fentanyl (27; group BLAO) *vs.* epidural ropivacaine (28; group LA), continuous postoperative infusion (all patients had access to PCA IV morphine postoperatively as needed)	B5	RLAO *vs.* LA ↓ m NS r BLAO *vs.* LA NS r m	NS r m	NS r m	–	Reduced morphine consumption in RLAO *vs.* LA at 2, 6 and 36 h, NS at 12, 24 and 48 h; and in BLAO *vs.* LA at 48 h, NS at 2, 6, 12, 24 and 36 h	**Qualitative outcomes** Reduced incidence of nausea and vomiting.[71] Incidence of sedation, pruritus: NS.[71]
Thoracic epidural opioid plus LA* versus *thoracic epidural LA plus systemic opioid								
[72]Harbers *et al*. 1991	Epidural infusion sufentanil (13) *vs.* IV infusion sufentanil (14) (both groups received epidural infusion bupivacaine)	B4	NS r	NS r	NS r	NS r	NS sufentanil use	**Qualitative outcomes** Incidence of nausea and/or vomiting, pruritus and pulmonary complications: NS.[72]
[73]Jacobson *et al*. 1983	Epidural bolus diamorphine (8) *vs.* IM injection diamorphine (10), administered on Day 1 postoperatively; both groups received epidural infusion bupivacaine	B4	–	NS r m	–	–	–	

↓ = significant benefit of epidural LA + opioid for reducing pain scores ($p<0.05$), compared with epidural LA with or without systemic opioid, on at least one time point on days 0 to 3 postoperatively, as indicated; r = at rest; m = on movement; NS = not significant; IV = intravenous; PCA = patient controlled analgesia; – = not recorded

Table S Thoracic epidural LA *versus* thoracic epidural opioid

Study	Thoracic epidural LA (LA) *vs.* thoracic epidural opioid (O) (number of patients)	Quality score	Pain (LA *vs.* O)				Supplementary analgesic use (LA *vs.* O)	Complications and adverse effects: quantitative outcomes (OR) and qualitative outcomes (LA *vs.* O)
			Day 0	Day 1	Day 2	Day 3		
Thoracic epidural LA* versus *epidural opioid								
[74]El-Baz, 1984	Thoracic epidural injections of bupivacaine as requested (30; group LA) *vs.* epidural morphine injections as requested (30; group O) *vs.* continuous epidural infusion of morphine with supplemental IV morphine as needed (30; group CO), all administered over 72 h postoperatively	B5	NS r over 72 h study Duration of analgesia over 72 h O>LA				–	**Quantitative outcomes** **Incidence of pruritus:** NS[4,74] 0.17 [0.00, 9.21], p=0.39 **Qualitative outcomes** Incidence of hypotension: NS;[4] higher incidence of hypotension in LA.[74] Incidence of nausea/vomiting: NS.[4] Incidence of urinary retention: NS.[74]
[4]Logas, 1987	Thoracic epidural bupivacaine (10) *vs.* epidural morphine (12), infusion started after induction and continued postoperatively (infusion rate increased postoperatively or IM morphine administered if analgesia inadequate)	A4	Similar r	Similar r	Reduced r in O	Reduced r in O	NS supplemental morphine use or total supplemental + epidural analgesic use	
			(no statistical analyses)					
[56]Scheinin, 1987	Thoracic epidural bupivacaine (10) *vs.* thoracic epidural morphine (8), infused intraoperatively and continued postoperatively (patients received IM oxycodone postoperatively as needed)	B1	NS r	NS r (at 24 h)	–	–	NS oxycodone use	

↓ = significant benefit of epidural LA for reducing pain scores ($p<0.05$) on at least one time point on days 0 to 3 postoperatively, as indicated, compared with epidural opioid; r = at rest; m = on movement; NS = not significant; IM = intramuscular; – = not recorded

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