reference	participants' characteristics	intervention group/ control group	outcomes
Momenzadeh et al. 2011 The role of intercostal cryoanalgesia in post-thoracotomy analgesia. Acta Med Iran. 2011;49(4):241-5.	**inclusion criteria** - age 19–51 yrs - ASA physical status I–III **exclusion criteria** - use of opioids or any other illegal drugs - drug addicts - diabetics who have had the disease for more than 10 yrs **demographic data mean±SD**: group C group CA p age (yrs) 41.3±15 41.9±16 NS sex (m/f) 15/15 25/5 <0.01 weight (kg) 64.7 ±10.6 64.1±12.1 NS site of thoracotomy - right 22 (73.3%) 19 (63.3%) NS - left 8 (26.7%) 11 (36.7%) ASA class I 4 (13.3%) 3 (10.0%) NS II 25 (83.4%) 27 (90.0%) III 1 (3.3%) 0 **patient flow and follow up:** total patient number included: 60 randomised in: group C: 30 group CA: 30 excluded: not reported analysed: 60 follow-up: 1 week, 1, 2, 3 months	**intervention prior to anaesthesia** - midazolam (2 mg/kg BW) - fentanyl (3 mg/kg BW) **mode of anaesthesia** - atracurium/fentanyl **surgical approach** - thoracotomy via posterolateral incisions **at the end of surgery** - group C (control): no cryoanalgesia - group CA (cryoanalgesia): before closure of the thorax, the intercostal nerves received a 90-second application of cold CO_2 (-70°C) **postoperative analgesia** - pethidine (0.5–1 mg/kg)	**postoperative pain [VAS 0-1 (no pain to mild), 2-3 (moderate), 4-10 (severe), %]:** - on day 2 postop the “severe” pain was observed in 33.3% and 0 of group C and group CA - on day 7 postop, the "no to mild pain" category was observed in 13.3% and 83.3% of group C and group CA respectively - intensity of pain in the control group was higher than the cryoanalgesia group throughout the follow-up period (p<0.01) **total dosage of pethidine in 24 h [mg]: mean±SD** group C group CA p 151.6± 27 87±48 p<0.001 **adverse effects/ events: n%** - hypoesthesia in group CA: % week 1 90 month 1 76.7 month 2 16.6 month 3 0
Sepsas et al. 2013 The role of intercostal cryoanalgesia in post-thoracotomy analgesia. Interact Cardiovasc Thorac Surg. 2013;16(6):814-8.	**inclusion criteria** - not reported **exclusion criteria** - ASA physical status ≥IV - age >75 yrs	**intervention prior to anaesthesia** - not reported **mode of anaesthesia** - fentanyl **surgical approach**	**postoperative pain [VAS] at rest: mean (±SD)** h group A group B p 6 0.9±0.7 (2,0) 3.00±1.00 (5,2) <0.001 12 0.8±0.55 (2,0) 2.4±0.5 (3,2) <0.001 18 0.8±0.5 (2,0) 2.5±0.9 (5,2) <0.001

reference	participants' characteristics	intervention group/ control group	outcomes
	- BMI >35 - history of other malignancy, - suffering from sleep apnoea - refusal to give informed consent **demographic data**: group A group B p sex (m/f) 21/4 21/4 0.6 ASA (1/2/3) 8/13/4 8/16/1 0.3 age (yrs) 64.4±7.1 64.8±8.6 0.9 weight (kg) 80.6±15.4 77.5±11.9 0.4 height (m) 1.73±0.07 1.70±0.07 0.5 **patient flow and follow up:** total patient number included: 50 randomised in: group A: 25 group B: 25 excluded: not reported analysed: 50 follow-up: 0, 6, 12, 18, 24 (1 day), 36, 48, 60, 72, 84, 96 h, 5, 6, 7, 14 days, 1 and 2 months	- thoracotomy + pulmonary resection (lobectomy, bilobectomy, pneumonectomy) **at the end of surgery** - group A (the study group): one session of cryoanalgesia (−40°C) for 60 s, under direct vision - group B patients (the control group): PCA morphine 1 mg/10 min only **rescue analgesia** - if VAS >3–5: IV morphine 2.5 mg/10 min **postoperative analgesia** IV morphine 0.3 mg/kg, tenoxicam 16 mg, paracetamol 2 g, 30 min before the end of the surgical procedure	24 0.6±0.6 (2,0) 2.45±1.2 (6,1) <0.001 36 0.4±0.5 (1,0) 2.6±1.1 (4,1) 0.002 48 0.5±0.5 (1,0) 2.1±0.95 (5,1) <0.001 60 0.1±0.35 (1,0) 1.6±0.5 (2,1) <0.001 72 0.4±0.5 (1,0) 1.6±0.8 (4,1) <0.001 84 0.1±0.3 (1,0) 1.3±0.7 (2,0) <0.001 96 0.25±0.4 (1,0) 1.4±0.7 (3,0) <0.001 Days 5 0.2±0.4 (1,0) 1.4±0.7 (3,0) <0.001 6 0.2±0.4 (1,0) 1.3±0.6 (3,0) <0.001 7 0.1±0.3 (1,0) 1.2±0.6 (3,0) <0.001 14 0.04±0.2 (1,0) 1.2±1.0 (3,0) <0.001 30 0.0±0.0 (0,0) 1.0±1.1 (3,0) <0.001 60 0.0±0.0 (0,0) 0.25±0.45 (1,0) 0.01 - group A patients had reduced levels of pain during quiet breathing and similar levels during coughing at all time points evaluated during the early (h 0–96) and late (days 5–60) postoperative period **dosage of morphine up to 96 h [mg]: mean±SD** Time (h) group A group B p 0 0.0±0.0 1.25±2.6 0.03 0–6 2.55±1.55 12.0±2.9 <0.001 6–12 2.25±1.3 11.1±3.5 <0.001 12–18 1.9±1.2 11.4±3.5 <0.001 18–24 1.75±1.0 10.7±2.5 <0.001 24–36 1.55±0.9 10.1±2.6 <0.001 36–48 1.6±1.05 10.3±3.1 <0.001 48–60 1.25±0.8 9.1±2.0 <0.001 60–72 0.65±0.7 9.5±2.3 <0.001 72–84 0.15±0.3 9.0±1.9 <0.001 84–96 0.05±0.2 8.1±1.5 <0.001 - significantly decreased consumption of morphine delivered through PCA pump by group A patients during the early postoperative period **analgesic requirement in late postop period (24 h dosage)** Day group A group B p 0 TR CD PC CL 0 TR CD PC CL 5 7 2 13 16 0 0 3 25 25 24 <0.001 6 9 0 12 16 0 0 6 23 23 21 <0.001 7 14 0 6 11 0 0 6 19 19 20 <0.001 14 17 0 1 7 0 0 8 14 25 2 <0.001 30 25 0 0 0 0 0 1 8 16 0 <0.001

reference	participants' characteristics	intervention group/ control group	outcomes
			60 25 0 0 0 0 7 3 15 15 0 <0.001 0 = none; TR = tramadol 200 mg; CD = codeine 90 mg; PC = paracetamol 1.5 g; CL = celecoxib 400 mg. - significantly decreased consumption of oral analgesics in group A during the late postoperative period **adverse effects/ events: n (%)** - nausea was more frequent in group B patients (20%) compared with group A patients (0%) between 12 and 18 h postop - vomiting was equally present in both groups. - no patient demonstrated nausea or vomiting after h 24 and 18 respectively
Khanbhai et al. 2013 Is cryoanalgesia effective for post-thoracotomy pain? Interact Cardiovasc Thorac Surg. 2014;18(2):202-9.	**databases/ search engines** - PubMed **search terms** - 'thoracotomy' OR ('thoracotomy [MeSH Terms]) AND 'cryoanalgesia' OR ('cryoanalgesia' [MeSH Terms]). **search period** - 1948 to December 2012 **inclusion criteria** - randomised control studies - in the English language **exclusion criteria** - none reported **included studies (n participants)** 1. Momenzadeh et al. 2011 (60) 2. Mustola et al. 2011 (42) 3. Ju et al. 2008 (107) 4. Yang et al. 2004 (80) 5. Gwak et al. 2004 (50) 6. Moorjani et al. 2001 (200) 7. Miguel et al. 1993 (45) 8. Muller et al. 1989 (63) 9. Roberts et al. 1988 (144) 10. Roxburgh et al. 1987 (53) 11. Rooney et al. 1986 (75) 12. Katz et al. 1980 (24)	1. Momenzadeh et al. 2011 - study group (30): cryoanalgesia + PRN pethidine - cryoanalgesia used at three intercostal nerves for 90 s at −70°C using CO_2 - control group (30): PRN pethidine 2. Mustola et al. 2011 - study group (21): thoracic epidural + cryoanalgesia at three intercostal nerves for 90 s at −70°C 10 cm from the nerve root - control group (21): epidural only 3. Ju et al. 2008 - study group (53): intercostal nerve cryoanalgesia at three intercostal nerves for 90 s at −70°C using CO_2 - control group (54): epidural analgesia 4. Yang et al. 2004 - study group (40): cryoanalgesia + epidural analgesia - cryoanalgesia used at three intercostal nerves for 90 s at −20°C using nitrous oxide - control group (40): epidural analgesia only 5. Gwak et al. 2004 - study group (25): IVCA + cryoanalgesia at three intercostal nerves for 90 s at −20°C using nitrous oxide - control group (25): IVCA 6. Moorjani et al. 2001 - study group (100): cryoanalgesia at three intercostal nerves for 60 s at −50°C using CO_2 - control group (100): conventional analgesia 7. Miguel et al. 1993 - study group (14): cryoanalgesia at three intercostal nerves for 30 s at −56.7°C - control group I (10): epidural morphine - control group II (11): parenteral morphine	1. Momenzadeh et al. 2011 - day 2 postop, VAS score of 10: • 33% of the control group • 0% of the study group, p<0.001 - day 7 postop VAS score of 0: • 13.3% control group • 83.3% study group, p<0.001 - day 1 postop: • control group, 151.6±27 • study group, 87±48, p<0.001 - pethidine required for: • 7 days in the control group • 4 days in the study group - hypoesthesia: • 90% at the end of first postop week • 76.7% at the end of first month • 16.6% at the end of third month - allodynia and dysesthesia: 10% at the end of first month 2. Mustola et al. 2011 Pain (VAS 0-3) At 12 h postop: • study group (VAS at rest), 18.6±17.8 • control group, 6.4±9.8, p=0.021 2 days: • study group (VPS at rest), 0.70±0.66 • control group, 0.15±0.37, p=0.017 8 weeks: • study group (VPS on movement), 1.10±1.04 • control group, 0.48±0.60, p=0.048 8 weeks postop: Allodynia • study group (11) • control group (4), p=0.048 Hypoesthesia • study group (20) • control group (10), p=0.0004 Epidural infusion rate (mL/h) • study group, 4.7±0.6 • control group, 5.1±0.5, not significant Number of boluses • study group, 6.2±4.9

reference	participants' characteristics	intervention group/ control group	outcomes
		- control group III (10): intrapleural analgesia 8. Muller et al. 1989 - study group (30): cryoanalgesia at four intercostal nerves with nitrous oxide until a ball of ice formed around the entire nerve - control group (33): no treatment 9. Roberts et al. 1988 - study group (71): cryoanalgesia at five intercostal for 30 s and repeated for a further 30 s at −60°C using nitrous oxide - control group (73): bupivacaine-adrenaline intercostal blockade 10. Roxburgh et al. 1987 - study group (23): cryoanalgesia and lumbar epidural methadone - control group (30): lumbar epidural methadone only 11. Rooney et al. 1986 - study group (25): cryoanalgesia at five of six intercostal nerves centred on the nerve of incision site, 60 s at −60°C - control group I (25): TNS - control group II (25): no treatment 12. Katz et al. 1980 - study group (15): cryoanalgesia at five intercostal nerves for 30 s at −60°C followed by 5 s thaw and second freeze-thaw cycle - control group (9): either intercostal blocks or no nerve-blocks	• control group, 5.8±4.7, not significant Oxycodone requirement (mg/3 days) • study group, 23.1±27.1 • control group, 38.4±66.9, not significant - study group (21): thoracic epidural + cryoanalgesia at three intercostal nerves for 90 s at −70°C 10 cm from the nerve root - control group (21): epidural only 3. Ju et al. 2008 Incidence of chronic pain: - no significant difference between the two groups Incidence of allodynia-like pain - significant difference found at 6 and 12 months, respectively: • study group, 7/43 (16.3%) • control group, 1/48 (2.1%), p=0.044 • study group, 6/39 (15.4%) • control group, 0/38 (0%), p=0.025 No pain or mild pain - significant difference found at 6 months: • study group, 31/43 (72.1%) • control group, 45/48 (93.7%), p=0.013 Moderate-to-severe pain No significant difference between the two groups Interference with daily life - significant difference found at 3, 6 and 12 months, respectively: • study group, 18/48 (37.5%) • control group, 6/50 (12.0%) p=0.003 • study group, 15/43 (34.9%) • control group, 5/48 (10.4%), p=0.005 • study group, 13/39 (33.3%) • control group, 3/38 (7.9%), p=0.005 Propofol and fentanyl dose - significantly higher in the study group, p<0.05 4. Yang et al. 2004 Pain at rest (VAS [median]) - no significant difference between the two groups Pain on movement (VAS [median]) - significant difference found on day 7 only: • study group, 1.9 • control group, 3.3, p=0.036 Rescue dose (median) of IV morphine - significant difference found on days 6 and 7, respectively: • study group, 3.9 • control group, 7.0, p=0.044 • study group, 3.2 • control group, 5.5, p=0.018 Changes in FEV_1 (%) - no significant difference between the two groups Changes in FVC (%) - significant difference found on day 7 only: • study group, 52 • control group, 46, p=0.024 Incidence of pain and numbness reported 1, 3 and 6 months postop - no significant difference between the two groups Incidence of post thoracotomy pain syndrome at rest at 1, 3 and 6 months - significant difference found at 3 months only: • study group, n=15 • control group, n=6, p=0.042

reference	participants' characteristics	intervention group/ control group	outcomes
			5. Gwak et al. 2004 Pain at rest and on movement (VAS) - no significant difference between the two groups Fentanyl (median [µg]) requirement - no significant difference between the two groups FEV_1 (mean [l]) and FVC (mean [l]) were evaluated preop, 2 and 7 days postop - significant difference found on day 7 only: - FEV_1 • study group, 1.8 • control group, 1.5, p<0.05 - FVC • study group, 2.25 • control group, 1.9, p<0.05 Incidence of pain and numbness at 1, 3 and 6 months postop - no significant difference between the two groups 6. Moorjani et al. 2001 Pain (VAS) each day for 7 days postop - days 1–7, respectively; study vs control group: • 3.8 vs 6.4 • 4.5 vs 7.4 • 3.1 vs 5.4 • 2.4 vs 3.6 • 0.2 vs 4.1 • 0.9 vs 2.1 • 0.1 vs 1.0, p<0.05 Additional opiate (mg) requirements - significantly lower use of opiates in study group compared with the control group, p<0.05 FEV_1 (% predicted) and FVC (% predicted) - no significant difference between the two groups 7. Miguel et al. 1993 Pain (VAS) each day for 5 days postop - no significant difference in pain scores with cryoanalgesia compared with controls Amount of breakthrough morphine - no significant difference between the groups Spirometry pre- and postop - no significant difference between the groups 8. Muller et al. 1989 Pain - no significant difference between the groups Mobility scores - no significant difference between the groups Analgesic consumption of opiates and non-opiates - no significant difference between the groups Peak expiratory flow (% of preoperative value) - no significant difference between the groups 9. Roberts et al. 1988 Pain (VAS [median]) postop - study vs control group: • 6–8 h, 1 vs 3 • 1 day, 4 vs 7 • 2 days, 2 vs 5 • 3 days, 2 vs 5, p<0.05 Pain (VAS [median]) during physiotherapy - study vs control group: • 1 day, 6 vs 7 • 2 days, 6 vs 8 • 3 days, 4 vs 7, p<0.05

reference	participants' characteristics	intervention group/ control group	outcomes
			Pethidine (mg [median]) administered after thoracotomy - study vs control group: • day 1, 145 vs 225, p<0.05 • day 2, 50 vs 200, p<0.01 • day 3, 0 vs 100, p<0.01 Patients (%) given oral analgesics administered after thoracotomy - study vs control group: • 0–2 days, 65 vs 14 • 3–5 days, 31 vs 73, p<0.01 *Pain related postop complications (study vs control group)* Patients (%) with stagnant bronchial secretions requiring bronchoscopy - 1.4 vs 15, p<0.05 Patients (%) requiring local block(s) - 6 vs 16, p<0.05 Patients (%) with late intercostal neuralgia 0 vs 3, not significant 10. Roxburgh et al. 1987 Pain (linear analogue scale) each day post-thoracotomy until discharge and 6 weeks and 6 months after discharge - no significant difference between two groups 11. Rooney et al. 1986 Preop and postop (Days 1 and 5) levels of FVC and FEV_1 (l [mean]) *FVC* - study vs control group I: Preoperative • 3.74±0.71 vs 3.24±0.64 Postoperative • - day 1, 1.27±0.30 vs 1.65±0.54, p<0.01 • - day 5, 2.20±0.61 vs 1.98±0.49, not significant - study vs control group II: Preoperative • 3.74±0.71 vs 3.77±0.83 Postoperative • - day 1, 1.27±0.30 vs 1.42±0.36, not significant • - day 5, 2.20±0.61 vs 1.86±0.33, p<0.001 *FEV_1* - study vs control group I: Preoperative • 2.78±0.79 vs 2.48±0.60 Postoperative • - day 1, 1.06±0.20 vs 1.30±0.46, p<0.01 • - day 5, 1.89±0.65 vs 1.54±0.50, not significant - study vs control group II: Preoperative 2.78±0.79 vs 2.86±0.63 Postoperative • - day 1, 1.06±0.20 vs 1.20±0.31, not significant • - day 5, 1.89±0.65 vs 1.60±0.32, p<0.01 12. Katz et al. 1980 *Pain* (10-point score; 1–3, slight pain, 4–6 moderate pain and 7–10 severe pain) - study vs control group: • day 1, 2.8 vs 6.0, p<0.001 • day 3, 1.8 vs 2.3, p<0.05 • day 5, 0.92 vs 3.2, p<0.01 *Narcotic usage* - study vs control group: • 15±2.3 vs 29±4.5, p<0.01 *Postoperative pulmonary function* - no significant difference between two groups