

Is Intravenous Patient Controlled Analgesia Enough for Pain Control in Patients Who Underwent Thoracoscopy?

This prospective randomized study was conducted to evaluate the efficacy of two common analgesic techniques, thoracic epidural patient-controlled analgesia (Epidural PCA), and intravenous patient-controlled analgesia (IV PCA), in patients undergoing lobectomy by the video-assisted thoracic surgical (VATS) approach. Fifty-two patients scheduled for VATS lobectomy were randomly allocated into two groups: an Epidural PCA group receiving an epidural infusion of ropivacaine 0.2%+fentanyl 5 μ g/mL combination at a rate of 4 mL/hr, and an IV PCA group receiving an intravenous infusion of ketorolac 0.2 mg/kg+fentanyl 15 μ g/mL combination at a rate of 1 mL/hr. Pain scores were then recorded using the visual analogue scale at rest and during motion (VAS-R and VAS-M, 0-10) for five days following surgery. In addition, we measured the daily morphine consumption, forced vital capacity (FVC), forced expiratory volume in 1 second (FEV₁), satisfaction score, and the incidence of side effects. Thirty-seven patients out of 52 completed the study (18 in the Epidural PCA group, 19 in the IV PCA group). There were no differences in the pain scores, analgesic requirements, pulmonary function, satisfaction score, and the incidence of side effects between groups. This indicates that IV PCA and Epidural PCA are equally effective to control the postoperative pain after VATS lobectomy, which suggests that IV PCA may be used instead of Epidural PCA.

Key Words : Analgesia, Patient-Controlled; Pain Measurement; Thoracic Surgery, Video-Assisted

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INTRODUCTION

Video-assisted thoracic surgery (VATS), which is known to be less invasive than conventional thoracotomy, causes less pain and better preservation of pulmonary function (1-4). However, patients can still experience considerable pain following VATS (5, 6). There are several studies to compare the efficacy of different analgesic methods in patients undergoing conventional thoracotomy. It has been demonstrated that thoracic epidural analgesia is more effective than systemic opioids in terms of pain relief (7, 8) or preservation of spirometric function (9). But there are few studies to compare the efficacy of different analgesic methods in patients undergoing VATS. It is well known that the thoracic epidural technique has the risk of dura puncture, epidural hematoma, nerve damage, and unsuccessful catheter placement (10, 11). Administration of intravenous (IV) patient controlled analgesia (PCA) is less invasive than epidural PCA, therefore, IV PCA would be preferable if it has similar analgesic effect compared to epidural PCA. Therefore, we conducted this prospective study to compare the efficacy of IV PCA and epidural PCA for the management of postoperative pain caused by VATS.

MATERIALS AND METHODS

After receiving approval from the Institutional Review Board and written, informed consent, 52 patients with lung cancer scheduled to undergo VATS lobectomy were enrolled. Patients with significant pre-operative pulmonary dysfunction, severe cardiovascular, hepatic, renal, musculo-skeletal disease, or more than 75-yr-old patients were excluded.

A computer-generated table was used to randomly assign the patients into two groups of 26: the Epidural PCA group and the IV PCA group. Patients in the Epidural PCA group had an epidural catheter that was inserted between 5th and 6th thoracic vertebra or 6th and 7th prior to the induction of anesthesia. We excluded intravascular or intrathecal catheter placement with a test dose of 3 mL lidocaine (2%) with 1:200,000 epinephrine.

All patients received the 5 mg/kg of thiopental sodium, IV, followed by 2 μ g/kg of fentanyl, and 0.1 mg/kg of vecuronium. A left-sided double-lumen endobronchial tube (Broncho-Cath™, Mallinckrodt, Athlone, Ireland) was inserted into all patients and anesthesia was then maintained with sevoflurane 2-4 vol% in a mixture of 50% oxygen and 50% air. Ex-

cept for opioids used at induction of anesthesia, initial loading of PCA, and continuous infusion of PCA, no additional opioids were administered during the maintenance of anesthesia. All operations were performed by one surgeon using same technique. The first analgesia dose was administered immediately after induction of anesthesia. In the Epidural PCA group, a 6 mL bolus of ropivacaine (0.2%) with 50 μ g fentanyl was administered via the epidural catheter ten minutes prior to surgical incision. Immediately after this, an epidural infusion of 2,500 μ g of fentanyl in 500 mL of 0.2% ropivacaine was started through the epidural catheter at a basal infusion rate of 4 mL/hr with an Abbott infusion pump (Aim[®]plus, Abbott Laboratories, U.S.A.). In the IV PCA group, a bolus of 1 μ g/kg fentanyl (Guju Pharm., Hwaseong, Korea) with 0.2 mg/kg ketorolac was administered prior to surgery. Immediately after this, intravenous infusion of 1,500 μ g of fentanyl with 300 mg of ketorolac in 100 mL of normal saline was started at a basal infusion rate of 1.0 mL/hr with an IV infusion pump (AutoMed[®]3200, Ace Medical, Korea). The analgesic bolus of PCA (using a 3 mL bolus and a lock-out time of 15 min in the Epidural PCA group and using a 1.0 mL bolus and a lock-out time of 15 min in the IV PCA group) was not administered during the operation, and started at postanesthesia care unit (PACU) by the patient after awakening.

The patient's pain intensity both at rest and during movement (VAS-R, VAS-M) was measured using a 10 cm non-graduated visual analogue scale at PACU one hour after operation and then daily for the first five days following surgery. Breakthrough pain that occurred during this period was treated by intravenous administration of 4 mg of morphine by nurses on demand. Total administered morphine doses were recorded, along with the incidence of nausea, vomiting, somnolence, dizziness, and pruritus. The incidence of respiratory depression, which was defined as a respiratory rate of <ten breaths/min, was also recorded.

In addition, the forced vital capacity (FVC) and forced expired volume in 1 second (FEV₁) were measured at the preoperative visit and again on the first, second, and third postoperative days using a portable spirometer (Micro, Micro Medical Limited, Rochester, U.K.). Three measurements were taken on each day with the patient in a sitting position. The FVC and FEV₁ recovery rates were expressed by determining the percentage of predicted values that were calculated based on number of resected pulmonary segments (1). Postoperative chest radiography were also taken for five days, and the incidence of atelectasis and pneumonia were recorded.

The patients were then asked to rank their satisfaction regarding their pain management on the fifth postoperative day according to the following scale: 0=very unsatisfactory, 1=unsatisfactory, 2=neutral, 3=satisfactory, 4=very satisfactory. All postoperative assessments were performed by one technician who did not know the purpose of this study.

An a priori- power analysis with a power of 80% and a Type

I error of 5% was conducted to determine the number of patients in each group that would be required to detect a 3 mg difference in the morphine requirement with an assumed standard deviation (SD) of 3. The results of this analysis indicated that seventeen patients per group would be required to detect such a difference, therefore, 26 patients were enrolled into each group because the dropout rate during the postoperative follow up was assumed to be 35% in the previous other study.

The patient characteristics between two groups were compared using a Student's t-test. Differences in the incidence of side-effects were compared using the chi-square test or Fisher's exact test. The VAS scores, the daily dose of rescue analgesic drugs and spirometry data were compared using two-way repeated-measures ANOVA, with the Holm-Sidak test being used for intragroup comparisons. The data are presented as mean \pm SD or number where appropriate. A probability of <0.05 was considered to be significant and Jandel Sigma Stat (version 3.0, Jandel Corporation, San Rafael, CA, U.S.A.) was used for all statistical analyses.

RESULTS

Of the 52 patients enrolled, 37 completed the study (18 in Epidural PCA Group, and 19 in IV PCA Group). Five patients (three in the Epidural PCA group and two in the IV PCA group) were withdrawn because the operation was changed into thoracotomy to control bleeding. Four patients (one in the Epidural PCA group and three in the IV PCA group) were withdrawn because they received talc pleurodesis after operation. In addition, four patients (two in each group) asked to stop PCA because of severe nausea and vomiting. One patient in the Epidural PCA group did not complete the study because he underwent postoperative mechanical ventilation. Finally, one patient in the Epidural PCA group did not complete the study because of accidental removal of the epidural catheter.

There were no significant differences in the patient characteristics and operation data between the two groups (Table 1). The pain scores were not different between the two groups (Fig. 1) and the need for rescue analgesics over the entire ob-

Table 1. Characteristics and surgical data of the patients

Parameters	Epidural PCA (n=18)	IV PCA (n=19)
Age (yr)	52.3 \pm 8.3	52.4 \pm 13.7
Sex (male/female)	11/7	9/10
Body weight (kg)	63.3 \pm 7.9	62.4 \pm 11.7
Height (cm)	164.9 \pm 8.3	162.9 \pm 8.8
Op duration (min)	157 \pm 38	152 \pm 28

Values are mean \pm SD or number of patients. There are no significant differences between two groups.

IV, intravenous; PCA, patient-controlled analgesia; Op, operation.

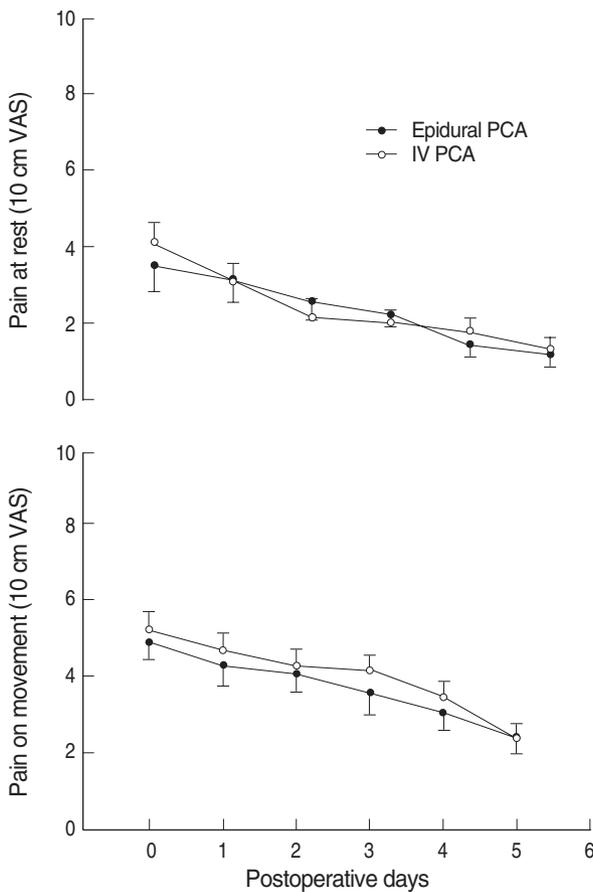


Fig. 1. Mean visual analogue scores (VAS) at rest and during movement. Error bars indicate standard error mean. There are no significant differences between two groups. IV, intravenous; PCA, patient-controlled analgesia.

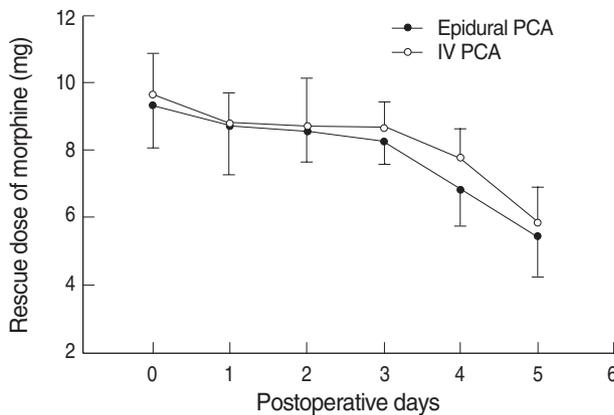


Fig. 2. Mean daily doses of intravenous morphine given as a rescue medication. Error bars indicate standard error mean. There are no significant differences between two groups. IV, intravenous; PCA, patient-controlled analgesia.

servation period was not different between the two groups (Fig. 2). Additionally, the percentage changes in the FVC and FEV₁ compared to the predicted values were similar in

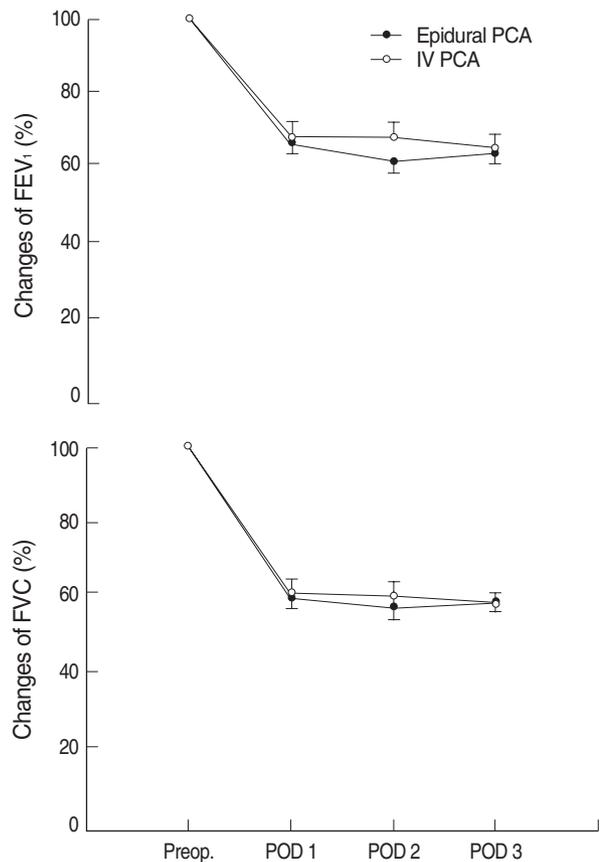


Fig. 3. Mean percentage changes in forced vital capacity (FVC) and forced expiratory volume in 1 second (FEV₁). Error bars indicate standard error mean. There are no significant differences between two groups.

IV, intravenous; PCA, patient-controlled analgesia; POD, post-operative day.

Table 2. Incidence of side-effects and postoperative complications

Symptoms/signs	Epidural PCA (n=18)	IV PCA (n=19)	P value
Dizziness	9 (50%)	11 (58%)	0.880
Somnolence	6 (33%)	10 (53%)	0.394
Pruritus	7 (39%)	6 (32%)	0.904
Nausea	4 (22%)	9 (47%)	0.209
Vomiting	2 (11%)	3 (16%)	0.948
Atelectasis	4 (22%)	6 (31%)	0.787
Pneumonia	1 (6%)	0 (0%)	0.977
Respiratory depression	0 (0%)	0 (0%)	1.000

Values are number of patients (percentages). There are no significant differences between two groups.

IV, intravenous; PCA, patient-controlled analgesia.

the two groups (Fig. 3). Furthermore, the average satisfaction score did not differ significantly (3.1 ± 0.7 in the Epidural PCA group, 3.2 ± 0.6 in the IV PCA group, respectively). Finally, the incidence of nausea, vomiting, dizziness, somno-

lence, pruritus, atelectasis, pneumonia, and respiratory depression were similar in the two groups (Table 2).

DISCUSSION

Patient-controlled thoracic epidural analgesia is the most effective mode of postoperative analgesia after thoracotomy (7). However, its use in less invasive VATS has not been widely explored. We investigated whether thoracic epidural analgesia has more benefit than IV PCA in postoperative pain management in patients undergoing VATS for primary lung cancer.

Our results suggest that the benefits of IV PCA in terms of the pain score, consumption of analgesics, restoration of pulmonary function, and satisfaction were equal to those of epidural PCA in patients undergoing VATS. Although these results do not agree with those of other studies that compared epidural PCA with IV PCA in patients who received thoracotomy (7-9), this may be due to different types of surgery. It is well known that VATS causes less tissue damage and respiratory dysfunction than thoracotomy (12, 13), therefore, the pain caused by VATS may be less severe and effectively controlled by IV PCA.

Based on this assumption, we reviewed previous studies that compared the use of IV PCA and epidural PCA in patients that underwent laparotomy, which is also assumed to cause less pain than thoracotomy. Aygun and colleagues (14) compared the effects of IV tramadol, IV fentanyl, epidural tramadol, and epidural fentanyl in patients that underwent lower abdominal surgery and found that adequate analgesia was achieved in all groups, but that IV tramadol and fentanyl were associated with a high incidence of nausea and vomiting. In our study, although there were slightly higher tendencies for nausea and vomiting in the IV PCA group, these differences were not significant.

We determined the analgesic regimen of each method referring to the most common and popular recommendations (15). According to a study comparing the efficacy of epidural and intravenous fentanyl administration using patient-controlled analgesia, pain scores and fentanyl plasma concentrations did not differ between the two routes of administration (16). In addition, Coda et al. (17) concluded that epidural administration of lipophilic opioids might offer no clinical advantage over the intravenous route. The amount of fentanyl administered in our study was not equal in two groups. We administered 20 $\mu\text{g/hr}$ of fentanyl in Epidural PCA group compared to 15 $\mu\text{g/hr}$ of fentanyl in IV PCA group because Geller et al. (18) had reported that more intense degree of sedation and the risk of respiratory depression was associated with intravenous sufentanil than epidural sufentanil. Therefore, we reduced the amount of fentanyl administered by intravenous route. We do not think the slight difference of the administered amount of fentanyl would affect the conclusion

of our study because the exact comparison of the efficacy of the route of administration was not the aim of our study.

Several methods for pain management after thoracoscopic surgery have been suggested. Perttunen et al. (5) reported that two-day IV infusion of diclofenac or ketorolac was effective to reduce total morphine consumption. Vogt et al. (19) and Hill et al. (20) have reported that a single-injection thoracic paravertebral block improved postoperative pain. Additionally, Ziser and others (21) attempted to determine the doses of parenteral analgesics administered after VATS retrospectively and found that 25.8 ± 11.6 mg/m² of morphine equivalent was administered during the first 24 hr, suggesting that higher opioid doses than previously anticipated were required. They also reported that patients of younger age, female gender, and use of patient-controlled analgesia received higher doses of analgesics. However, none of the above cited studies compared the recommended methods with the use of thoracic epidural PCA that has been known as most effective method, thus lacking the relative efficacy of the methods they elicited. When Furrer and co-workers (22) evaluated the use of epidural PCA for patients undergoing thoracotomy and IV PCA for patients undergoing thoracoscopy, respectively, they found that the pain score and restoration of pulmonary function were similar in both groups.

Some contradicting results regarding the efficacy of epidural analgesia after VATS have been reported. Fernandez and colleagues (23) reported that the use of a patient-controlled epidural analgesia in patients undergoing VATS pleurectomy was as effective as parenteral opioids, but did not confer any additional benefits to other less invasive methods of analgesia. This result is comparable to the results of the present study, however, the procedures used in their study involved more minimal access than those used in our study. Conversely, Yoshioka and others (24) reported that epidural analgesia is more effective than non-epidural analgesia for pain control until post-operative day (POD) 1 after VATS, especially for pain on movement. Based on their results, they recommended epidural analgesia be used until POD 1, but that other analgesic method should be employed beginning on POD 2 because of the high incidence of nausea and vomiting associated with epidural analgesia. However, in our study, we did not observe any differences in pain score or analgesic consumption between two groups even on POD 1.

The number of ports, the size and location of incision, and the duration of VATS can be varied considerably by the surgeons, so we included only the patients who received VATS from the most skillful surgeon to eliminate possible confounders. Three ports (4 cm, 10 mm, 5 mm) were used, scattered over two or three intercostal spaces. No ribs were resected and no rib-spread technique was used. The number of ports, size of incision, and duration of VATS were considerably lower than other studies (1, 4, 12). Not to use invasive method of surgery makes us to consider the change the methods of pain management to less invasive one.

Nakata et al. (4) reported that FVC and FEV₁ of the patients restored 85-90% of predicted values at POD 7. According to Furrer et al. (22), FVC and FEV₁ measured at POD 1 ranged 59-64% and nearly reached preoperative values at the time of discharge. Our patients recovered 60-70% of predicted value at POD 1 and did not show further improvement until POD 3. Because we did not check the FVC and FEV₁ after POD 3, direct comparison with above studies was impossible. The reason why we did not check the FVC and FEV₁ after POD 3 is that we assumed if the difference in restoration of pulmonary function between groups exist, it would appear in acute postoperative period.

Our study has several limitations. First, our study was not blinded because blinding was not practically possible. Second, we asked the pain scores 1 hr after operation and 24 hr after operation, but not between 1 hr and 24 hr after operation. Senagore and co-workers (25) reported improved pain control in a group that received epidural PCA when compared to that of a group that received parenteral opioids at 6 hr and 18 hr after laparoscopic segmental colectomy, but no alteration in the length of the hospital stay between groups. In addition, Perttunen et al. (5) or Yoshioka and others (24) also reported that patients who received VATS experienced moderate or severe pain immediately after operation and that epidural PCA was more effective at managing pain during this period. Therefore, in our study a difference in the two techniques may have occurred during this period and not been detected. However, we assume the difference was not great because the cumulative morphine consumption on POD 1 did not differ between two groups.

In conclusion, IV PCA is as equally effective as Epidural PCA in patients undergoing VATS lobectomy, therefore, it may replace Epidural PCA.

REFERENCES

- Nagahiro I, Andou A, Aoe M, Sano Y, Date H, Shimizu N. *Pulmonary function, postoperative pain, and serum cytokine level after lobectomy: a comparison of VATS and conventional procedure.* *Ann Thorac Surg* 2001; 72: 362-5.
- Landreneau RJ, Hazelrigg SR, Mack MJ, Dowling RD, Burke D, Gavlick J, Perrino MK, Ritter PS, Bowers CM, DeFino J, Nunchuck SK, Freeman J, Keenan RJ, Ferson PF. *Postoperative pain-related morbidity; video-assisted thoracic surgery versus thoracotomy.* *Ann Thorac Surg* 1993; 56: 1285-9.
- Li WW, Lee RL, Lee TW, Ng CS, Sihoe AD, Wan IY, Arifi AA, Yim AP. *The impact of thoracic surgical access on early shoulder function: video-assisted thoracic surgery versus posterolateral thoracotomy.* *Eur J Cardiothorac Surg* 2003; 23: 390-6.
- Nakata M, Saeki H, Yokoyama N, Kurita A, Takiyama W, Takashima S. *Pulmonary function after lobectomy: video-assisted thoracic surgery versus thoracotomy.* *Ann Thorac Surg* 2000; 70: 938-41.
- Perttunen K, Nilsson E, Kalso E. *I.v. diclofenac and ketorolac for pain after thoracoscopic surgery.* *Br J Anaesth* 1999; 82: 221-7.
- Kirby TJ, Mack MJ, Landreneau RJ, Rice TW. *Lobectomy-video-assisted thoracic surgery versus muscle-sparing thoracotomy. A randomized trial.* *J Thorac Cardiovasc Surg* 1995; 109: 997-1001.
- Sentürk M, Ozcan PE, Talu GK, Kiyan E, Camci E, Ozyalcin S, Dilgece S, Pembeci K. *The effects of three different analgesia techniques on long-term postthoracotomy pain.* *Anesth Analg* 2002; 94: 11-5.
- Miguel R, Hubbell D. *Pain management and spirometry following thoracotomy: a prospective, randomized study of four techniques.* *J Cardiothorac Vasc Anesth* 1993; 7: 529-34.
- Richardson J, Sabanathan S, Shah R. *Post-thoracotomy spirometric lung function: the effect of analgesia. A review.* *J Cardiovasc Surg (Torino)* 1999; 40: 445-56.
- Giebler RM, Scherer RU, Peters J. *Incidence of neurologic complications related to thoracic epidural catheterization.* *Anesthesiology* 1997; 86: 55-63.
- Christie IW, McCabe S. *Major complications of epidural analgesia after surgery: results of a six-year survey.* *Anaesthesia* 2007; 62: 335-41.
- Tajiri M, Maehara T, Nakayama H, Sakamoto K. *Decreased invasiveness via two methods of thoracoscopic lobectomy for lung cancer, compared with open thoracotomy.* *Respirology* 2007; 12: 207-11.
- Craig SR, Leaver HA, Yap PL, Pugh GC, Walker WS. *Acute phase responses following minimal access and conventional thoracic surgery.* *Eur J Cardiothorac Surg* 2001; 20: 455-63.
- Aygun S, Kocoglu H, Goksu S, Karaca M, Oner U. *Postoperative patient-controlled analgesia with intravenous tramadol, intravenous fentanyl, epidural tramadol and epidural ropivacaine+fentanyl combination.* *Eur J Gynaecol Oncol* 2004; 25: 498-501.
- Wu CL. *Acute postoperative pain.* In: Miller RD, editor, *Miller's Anesthesia. 6th ed. Volume 2.* Philadelphia: Elsevier Churchill Livingstone 2005; 2732-43.
- Glass PS, Estok P, Ginsberg B, Goldberg JS, Sladen RN. *Use of patient-controlled analgesia to compare the efficacy of epidural to intravenous fentanyl administration.* *Anesth Analg* 1992; 74: 345-51.
- Coda BA, Brown MC, Schaffer R, Donaldson G, Jacobson R, Hautman B, Shen DD. *Pharmacology of epidural fentanyl, alfentanil, and sufentanil in volunteers.* *Anesthesiology* 1994; 81: 1149-61.
- Geller E, Chrubasik J, Graf R, Chrubasik S, Schulte-Mönting J. *A randomized double-blind comparison of epidural sufentanil versus intravenous sufentanil or epidural fentanyl analgesia after major abdominal surgery.* *Anesth Analg* 1993; 76: 1243-50.
- Vogt A, Stieger DS, Theurillat C, Curatolo M. *Single-injection thoracic paravertebral block for postoperative pain treatment after thoracoscopic surgery.* *Br J Anaesth* 2005; 95: 816-21.
- Hill SE, Keller RA, Stafford-Smith M, Grichnik K, White WD, D'Amico TA, Newman MF. *Efficacy of single-dose, multilevel paravertebral nerve blockade for analgesia after thoracoscopic procedures.* *Anesthesiology* 2006; 104: 1047-53.
- Ziser A, Messick JM, Schroeder DR, Allen MS. *Requirements for postoperative analgesics in patients undergoing video-assisted thoracic surgery.* *The Internet Journal of Anesthesiology* 1999; Vol3 N2 Available at <http://www.ispub.com/ostia/index.php?xmlFilePath=>

journals/ija/vol3n2/vats.xml

22. Furrer M, Rechsteiner R, Eigenmann V, Signer C, Althaus U, Ris HB. *Thoracotomy and thoracoscopy: postoperative pulmonary function, pain and chest wall complaints. Eur J Cardiothorac Surg 1997; 12: 82-7.*
23. Fernandez MI, Martin-Ucar AE, Lee HD, West KJ, Wyatt R, Waller DA. *Does a thoracic epidural confer any additional benefit following video-assisted thoracoscopic pleurectomy for primary spontaneous pneumothorax? Eur J Cardiothorac Surg 2005; 27: 671-4.*
24. Yoshioka M, Mori T, Kobayashi H, Iwatani K, Yoshimoto K, Terasaki H, Nomori H. *The efficacy of epidural analgesia after video-assisted thoracoscopic surgery: a randomized control study. Ann Thorac Cardiovasc Surg 2006; 12: 313-8.*
25. Senagore AJ, Delaney CP, Mekhail N, Dugan A, Fazio VW. *Randomized clinical trial comparing epidural anaesthesia and patient-controlled analgesia after laparoscopic segmental colectomy. Br J Surg 2003; 90: 1195-9.*