Veterinary Regional Anaesthesia and Pain Medicine
The Official Journal of ISVRA - the Italian Society of Veterinary Regional Anaesthesia and Pain Medicine
Available for free download at www.isvra.org

Levionnois O.

Pain after thoracic surgery

VRA 2008; 6(1):1-6

Dr Olivier Levionnois, DVM, DMV, Dipl.ECVAA: Clinical Anaesthetist, Anaesthesia Section, Department of Clinical Veterinary Medicine, Vetsuisse Faculty of the University of Berne, Berne, Switzerland.

Received from Department of Clinical Veterinary Medicine, Vetsuisse Faculty of the University of Berne, Berne, Switzerland. Submitted for pubblication October 6, 2008. Accepted for pubblication October 27, 2008.

Address correspondence to Dr Levionnois: Anaesthesia Section, Department of Clinical Veterinary Medicine, Vetsuisse Faculty of the University of Berne, Box Office 8466, CH-3001 Berne, Switzerland. E-mail: olivier.levionnois@kkh.unibe.ch

A. Gottschalk, S.P. Cohen, S. Yang, E.A. Ochroch
Preventing and Treating Pain after Thoracic Surgery
Anesthesiology 2006; 104:594–600

PAPER SUMMARY, COMMENTS AND COMPARATIVE ASPECTS

Thoracic trauma, diaphragmatic hernia, thymoma, oesophageal lesions, persistent right aortic arch, pulmonary lesions, chylothorax, pericardiectomy, patent ductus arteriosus, pulmonic or aortic stenosis … Those are the most known conditions motivating thoracic surgery in dogs and cats.[1] The surgical approach and the prognosis are definitely a great challenge in these conditions. But marked peri-operative pain may also make the anaesthesia at risk of cardio-respiratory instability and severe post-operative pain will complicate the monitoring of post-operative hypoxemia and the eventual administration of oxygen in a stressed animal, the tolerance of a chest drain and will prolong the return of a functional animal back home.

Gottschalk et al. pointed that people complain about severe pain after thoracotomy when appropriate analgesia is not warranted and discomfort may last for months to years even with adequate acute post-operative pain therapy. This is difficult to assess in animals but if thoracic pain and its main symptoms – dyspnea and/or hypoventilation – are commonly described, there are some notable differences. In humans, the sternotomy is attributed to lower levels of pain than lateral thoracotomy. In dogs, the opposite is generally observed. This may be explained by the different anatomy and the greater importance of the sternum in domestic animal than in humans to support the thorax. Active movements of the thoracic wall are also less involved in animals than in humans. Thus, pain and reduced lung function can be expected to be less induced by thoracic wall incision. Humans appear to experience marked pain even after thoracoscopic procedures probably due to intercostals nerve and muscle damage from trocar insertion, when dogs seem to benefit from less invasive thoracoscopic procedures as showing less post-operative discomfort and more rapid return to function.[2] However it should not be forget that animals presented with traumatic rib fractures generally present marked discom-

fort and pain provoking obvious dyspnoea which often improve with pain medication.

Like for any invasive and painful surgical procedure, the analgesic therapy should be aggressive, preemptive and multimodal. Besides an adequate level of general anaesthesia, this generally involves at least a solid loco-regional technique and the pre-, peri- and post-operative administration of opioids and non-steroidal anti-inflammatory drugs.

The gold standard of peri-operative loco-regional anaesthetic technique is described by Gottschalk et al. as the pre-operative placement of a thoracic epidural catheter to administer long-acting local anaesthetics at low concentrations together with lipophilic opioids. The main reason why this technique may sounds unfamiliar in many ways to veterinary practitioners is that the development of veterinary anaesthesia is way behind the practices of a human hospital (how unfortunate!) and the required skills and validation of this technique have still not been defined by veterinary leading institutions (universities and large private clinics). The placement and care of an epidural catheter in dogs and cats has been already well described.[3] Its placement at the thoracic level is a much less common procedure in veterinary clinics. However, the technique has been successfully described at many occasion in experimental studies[4] and even in clinical setting.[5] Briefly, under general anaesthesia, the epidural space is accessed under fluoroscopy at the L5-L6 inter-vertebral segment (loss-of-resistance technique, 16G Tuohy-needle) and a radiopaque epidural catheter is advanced cranially to the Th10-level. The final position of the catheter tip is confirmed by typical epidural spread of injected radiopaque dye (2 ml). The use of low concentrations of long-lasting local anaesthetics (bupivacaine, ropivacaine) targets the blockade of small and less myelinated nociceptive A-delta and C fibers to produce analgesia and minimal interaction with large motor fibers to limit functional motor blockade. Again, the practice of differential epidural blockade is poorly described in veterinary medicine but has been shown to be valid.[6-9] Finally, the epidural administration of lipophilic opioids (e.g. fentanyl), a standard in human medicine, is rarely described in clinical veterinary practice but has been proved effective.[10-12] According to their rapid diffusion and short duration of action, they should be administered as an infusion as close as possible to the site of action (thoracic level). Before the technique appears as a veterinary standard for thoracic surgeries, further prospective studies and clinical experiences are required from specialized and skilled veterinarians.

The logical consequence to this, is that alternative therapies proposed by Gottschalk et al. are the standard in veterinary pain therapy. Intravenous analgesics, intercostals nerve blocks,[13,14] intrapleural catheter[15-17] and wound infiltration with local anesthetics are commonly combined to obtain the best analgesic effect. The concern of the toxicity with high systemic reabsorption of the cumulative dose of lidocaine and/or bupivacaine should be addressed by calculating regularly the total dose administered and keeping it below 6 mg kg^{-1} via dilution with NaCl or buffering with a bicarbonate solution. Intravenous analgesics are typically non-steroidal anti-inflammatory drugs and high doses of opioids. If fentanyl is a standard for continuous pre-, peri- and post-operative intravenous infusion, morphine or methadone can also be administered as an infusion[18,19] or by repeated boli. The additional use of ketamine and/or lidocaine intravenous infusions[20,21] is expected to enhance antinociception via other modes of action.

Adjustment of post-operative analgesic therapy is somehow facilitated in humans with patient-controlled analgesia. If this is not an option for our animals, the choice and dose of analgesics should at least be patient-oriented. This is only possible with regular evaluation of the animal for pain, stress and discomfort. The use of composite pain scales combining at least global subjective evaluation, behavioral modifications, interaction with the observer and wound palpation allow the veterinary practices to evaluate pain more objectively and comply with less experienced staff.[22] Like for humans, the animal will be sent back home as soon as the medical and surgical conditions are stable, but the further delivery of pain medication should not be stopped if signs of discomfort are still present. Quite intensive pain therapy may be maintained at home by using oral formulation of non-steroidal anti-inflammatory drugs, morphine, tramadol and gabapentin. Oriented observations by the owner and regular check-up may allow to progressively stop the analgesic therapy.

Finally, if thoracic epidural analgesia is not a common procedure, the alternative of administering pre- and post-operatively in the epidural space a single bolus of hydrophilic opioid (morphine) at the lumbo-sacral interspace has been proved clinically relevant to improve analgesia compared to systemic route[5,23-25] and is easily feasible. The combination of a preoperative intrathecal (spinal) bolus of fentanyl with bupivacaine together with the delivery of morphine and bupivacaine via an epidural catheter over the peri- and post-operative phase has also been described as an effective combined spinal-epidural analgesia in a dog.[12]

The association of preoperative non-steroidal anti-inflammatory drug, systemic opioid, intercostal nerve blocks and epidural analgesia, perioperative general anaesthesia, systemic opioid and eventually intravenous adjunct analgesia (ketamine and/or lidocaine), and post-operative intrapleural analgesia, repeated epidural analgesia and systemic opioids all together provide a powerful multimodal analgesic plan around thoracic surgery.[1] Particular post-operative persistent pain syndrome should be addressed with non-steroidals, opioids, tramadol, gabapentin and eventually ketamine according to symptoms and compliance of the owner.

References

1. Pascoe PJ. Thoracic surgery In: Seymour C, Duke T (Eds.): BSAVA Manual of Canine and Feline Anaesthesia and Analgesia. 2nd ed. Gloucester. British Small Animal Veterinary Association. (2007), pp230-243
2. Walsh PJ, Remedios AM, Ferguson JF, et al. Thoracoscopic versus open partial pericardectomy in dogs: comparison of postoperative pain and morbidity. Vet Surg 1999;28:472-479
3. Wetmore LA, Glowaski MM. Epidural analgesia in veterinary critical care. Clin Tech Small Anim Pract 2000;15:177-188

4. Schwarte LA, Picker O, Hohne C, et al. Effects of thoracic epidural anaesthesia on microvascular gastric mucosal oxygenation in physiological and compromised circulatory conditions in dogs. Br J Anaesth 2004;93:552-559
5. Kahn L, Baxter FJ, Dauphin A, et al. A comparison of thoracic and lumbar epidural techniques for post-thoracoabdominal esophagectomy analgesia. Can J Anaesth 1999;46:415-422
6. Feldman HS, Covino BG. Comparative motor-blocking effects of bupivacaine and ropivacaine, a new amino amide local anesthetic, in the rat and dog. Anesth Analg 1988;67:1047-1052
7. Feldman HS, Dvoskin S, Arthur GR, et al. Antinociceptive and motor-blocking efficacy of ropivacaine and bupivacaine after epidural administration in the dog. Reg Anesth 1996;21:318-326
8. Feldman HS, Dvoskin S, Halldin MH, et al. Comparative local anesthetic efficacy and pharmacokinetics of epidurally administered ropivacaine and bupivacaine in the sheep. Reg Anesth 1997;22:451-460
9. Skarda RT, Muir WW 3rd. Analgesic, behavioral, and hemodynamic and respiratory effects of midsacral subarachnoidally administered ropivacaine hydrochloride in mares. Vet Anaesth Analg 2003;30:37-50
10. Almeida TF, Fantoni DT, Mastrocinque S, et al. Epidural anesthesia with bupivacaine, bupivacaine and fentanyl, or bupivacaine and sufentanil during intravenous administration of propofol for ovariohysterectomy in dogs. J Am Vet Med Assoc 2007;230:45-51
11. Naganobu K, Maeda N, Miyamoto T, et al. Cardiorespiratory effects of epidural administration of morphine and fentanyl in dogs anesthetized with sevoflurane. J Am Vet Med Assoc 2004;224:67-70
12. Novello L, Corletto F. Combined spinal-epidural anesthesia in a dog. Vet Surg 2006;35:191-197
13. Berg RJ, Orton EC. Pulmonary function in dogs after intercostal thoracotomy: comparison of morphine, oxymorphone, and selective intercostal nerve block. Am J Vet Res 1986;47:471-474
14. Flecknell PA, Kirk AJ, Liles JH, et al. Post-operative analgesia following thoracotomy in the dog: an evaluation of the effects of bupivacaine intercostal nerve block and nalbuphine on respiratory function. Lab Anim 1991;25:319-324
15. Conzemius MG, Brockman DJ, King LG, et al. Analgesia in dogs after intercostal thoracotomy: a clinical trial comparing intravenous buprenorphine and interpleural bupivacaine. Vet Surg 1994;23:291-298
16. Thompson SE, Johnson JM. Analgesia in dogs after intercostal thoracotomy. A comparison of morphine, selective intercostal nerve block, and interpleural regional analgesia with bupivacaine. Vet Surg 1991;20:73-77
17. Dhokarikar P, Caywood DD, Stobie D, et al. Effects of intramuscular or interpleural administration of morphine and interpleural administration of bupivacaine on pulmonary function in dogs that have undergone median sternotomy. Am J Vet Res 1996;57:375-380
18. Guedes AG, Papich MG, Rude EP, et al. Pharmacokinetics and physiological effects of two intravenous infusion rates of morphine in conscious dogs. J Vet Pharmacol Ther 2007;30:224-233
19. Lucas AN, Firth AM, Anderson GA, et al. Comparison of the effects of morphine administered by constant-rate intravenous infusion or intermittent intramuscular injection in dogs. J Am Vet Med Assoc 2001;218:884-891
20. Muir WW, 3rd, Wiese AJ, March PA. Effects of morphine, lidocaine, ketamine, and morphine-lidocaine-ketamine drug combination on minimum alveolar concentration in dogs anesthetized with isoflurane. Am J Vet Res 2003;64:1155-1160
21. Solano AM, Pypendop BH, Boscan PL, et al. Effect of intravenous administration of ketamine on the minimum alveolar concentration of isoflurane in anesthetized dogs. Am J Vet Res 2006;67:21-25
22. Morton CM, Reid J, Scott EM, et al. Application of a scaling model to establish and validate an interval level pain scale for assessment of acute pain in dogs. Am J Vet Res 2005;66:2154-2166
23. Popilskis S, Kohn D, Sanchez JA, et al. Epidural vs. intramuscular oxymorphone analgesia after thoracotomy in dogs. Vet Surg 1991;20:462-467
24. Dauphin A, Lubanska-Hubert E, Young JE, et al. Comparative study of continuous extrapleural intercostal nerve block and lumbar epidural morphine in post-thoracotomy pain. Can J Surg 1997;40:431-436
25. Pascoe PJ, Dyson DH. Analgesia after lateral thoracotomy in dogs. Epidural morphine vs. intercostal bupivacaine. Vet Surg 1993;22:141-147

Il dolore postoperatorio nella chirurgia toracica

Levionnois O.

A. Gottschalk, S.P. Cohen, S. Yang, E.A. Ochroch
Preventing and Treating Pain after Thoracic Surgery
Anesthesiology 2006; 104:594–600

BREVE RIASSUNTO, CONSIDERAZIONI E APPROCCIO COMPARATO

Un trauma toracico, un'ernia diaframmatica, un timoma, lesioni esofagee, la persistenza dell'arco aortico destro, lesioni polmonari, un chilotorace, una pericardiectomia, un dotto arterioso pervio, una stenosi aortica o polmonare … queste sono le cause più frequenti che richiedono una chirurgia toracica nel cane e nel gatto.[1] L'approccio chirurgico e la prognosi sono certamente una grande sfida in queste condizioni. Un dolore peri-operatorio marcato può anche rendere l'anestesia a rischio di instabilità cardio-respiratoria, e un grave dolore post-operatorio complicherà il monitoraggio dell'ipossemia post-operatoria e l'eventuale somministrazione di ossigeno in un animale stressato, la

tolleranza di un drenaggio toracico e prolungherà il ritorno a casa di un animale funzionale.
Gottschalk e colleghi hanno puntualizzato come le persone lamentano un dolore grave dopo una toracotomia quando non viene garantita una analgesia appropriata e il disagio può durare mesi o anni anche con una terapia adeguata del dolore acuto post-operatorio. Questo è difficile da quantificare negli animali, e se il dolore toracico e i suoi principali sintomi – dispnea e/o ipoventilazione – sono comunemente descritti, ci sono alcune differenze notevoli. Negli uomini, la sternotomia è collegata a livelli di dolore più bassi rispetto alla toracotomia laterale. Nei cani, si osserva generalmente l'opposto. Questo può essere spiegato dalla differente anatomia a dalla maggiore importanza svolta dallo sterno negli animali domestici rispetto che negli uomini nel supporto del torace. I movimenti attivi della parete toracica sono inoltre meno complessi negli animali piuttosto che negli uomini. Perciò ci si può aspettare che un'incisione della parete toracica causi un minor dolore e una minor ridotta funzionalità polmonare. Gli uomini sembrano sperimentare un dolore marcato perfino dopo procedure in toracoscopia, probabilmente a causa di lesioni dei nervi e dei muscoli intercostali derivate dall'inserzione del trocar, mentre i cani sembrano trarre beneficio dalle procedure toracoscopiche meno invasive come dimostrato dal minor disagio postoperatorio e dal più rapido recupero funzionale.[2] Comunque non bisogna dimenticare che gli animali che presentano fratture costali traumatiche generalmente mostrano un marcato disagio e dolore generanti, ovviamente, dispnea che però spesso migliora con il trattamento del dolore stesso.
Come per qualsiasi procedura chirurgica dolorosa ed invasiva, la terapia analgesica dovrebbe essere aggressiva, preventiva e multimodale. Questa generalmente comprende, accanto ad un adeguato livello di anestesia generale, almeno una solida tecnica loco-regionale e la somministrazione pre-, peri e post- operatoria di oppiodi e farmaci antinfiammatori non-steroidei.
La tecnica anestesiologica loco-regionale peri-operatoria ottimale è descritta da Gottschalk e colleghi come il posizionamento pre-operatorio di un catetere epidurale toracico per somministrare anestetici locali a lunga durata a basse concentrazioni insieme a oppiodi lipofilici. Questa tecnica può non suonare molto familiare ai veterinari perché lo sviluppo dell'anestesia veterinaria segue con molto ritardo (sfortunatamente) le esperienze cliniche degli ospedali umani e al momento nessuna delle strutture veterinarie all'avanguardia (Università e grandi cliniche private) ha validato clinicamente questa tecnica nè ha suggerito quali competenze siano richieste per la sua corretta esecuzione.
Mentre il posizionamento e la gestione di un catetere epidurale nel cane e nel gatto è stato già ben descritto,[3] il suo posizionamento a livello toracico in medicina veterinaria è una procedura assai rara.Comunque, la tecnica è stata descritta con successo in molte occasioni in studi sperimentali[4] e persino in alcuni pazienti clinici.[5] Brevemente, con il paziente in anestesia generale, si accede allo spazio epidurale a livello del segmento intervertebrale in fluoroscopia (tecnica della perdita di resistenza, aghi di Tuohy 16 G) e un catetere epidurale radiopaco viene fatto avanzare cranialmente a livello di T-10. La posizione finale della punta del catetere viene confermata dalla diffusione tipica epidurale di un liquido di contrasto radiopaco (2ml). L'uso di basse concentrazioni di anestetici locali di lunga durata (bupivacaina, ropivacaina) fa ottenere il blocco delle piccole e meno mielinizzate fibre nocicettiove A-delta e fibre C per produrre analgesia ed avere la minima interazione con le grosse fibre motrici e limitare così il blocco motorio funzionale. Di nuovo, il blocco differenziale è poco descritta in medicina veterinaria, ma si è comunque dimostrata valida.[6-9] Infine, la somministrazione epidurale di oppiodi lipofilici (ad es. fentanil), frequente in medicina umana, è raramente descritta nella pratica clinica veterinaria, anche se si è dimostrata efficace.[10-12] In relazione alla loro rapida diffusione e alla breve durata d'azione, dovrebbero essere somministrati in infusione il più vicino possibile al sito d'azione (a livello toracico). Tuttavia, prima che la tecnica diventi uno standard per la chirurgia toracica in veterinaria, sono necessari ulteriori studi ed esperienze cliniche da veterinari specializzati ed esperti.
La conseguenza logica di questo, è che le terapie alternative proposte da Gottschalk e colleghi sono le più utilizzate nella terapia antidolorifica in veterinaria. Analgesici intravenosi, il blocco dei nervi intercostali,[13,14] il catetere intrapleurico[15-17] e l'infiltrazione della ferita con anestetici locali sono associati comunemente tra loro per ottenere il miglior effetto analgesico. Il problema della tossicità legata all'elevato riassorbimento sistemico di dosi cumulative di lidocaina e/o bupivacaina dovrebbe essere gestita calcolando regolarmente la dose totale somministrata e mantenendola al di sotto di 6 mg kg^{-1} attraverso la diluizione con NaCl o tamponandola con soluzioni di bicarbonato. Tra gli analgesici endovenosi utilizzati troviamo tipicamente i farmaci antinfiammatori non steroidei e oppioidi a dosi elevate. Se il fentanil è uno standard per l'infusione endovenosa continua pre-, peri- e post-operatoria, anche la morfina o il metadone possono essere somministrati in infusione[18,19] o, in alternativa, in boli ripetuti. Si ritiene che l'uso in aggiunta di ketamina e/o lidocaina in infusione continua aumenti l'antinocicezione attraverso altre modalità d'azione.[20,21]
La regolazione della terapia analgesica post-operatoria è in qualche modo facilitata negli uomini dalla possibilità da parte del paziente di controllare direttamente il livello di analgesia. Se questa non è un'opzione per i nostri animali, la scelta e la dose degli analgesici dovrebbero almeno essere orientate al singolo paziente. Questo è possibile solo valutando regolarmente l'animale in relazione al dolore, allo stress e al disagio. L'uso di scale del dolore codificate insieme ad una valutazione soggettiva globale, ai cambiamenti nel comportamento del soggetto, alla sua interazione con l'osservatore e alla palpazione della ferita permette al veterinario di stimare il dolore in modo oggettivo e completo, anche in presenza di personale con esperienza limitata.[22] Come per gli uomini, l'animale sarà dimesso quando le condizioni mediche e chirurgiche saranno stabili, ma l'ulteriore somministrazione di antidolorifici non dovrebbe essere interrotta se sono ancora presenti segni di disagio. Una terapia antidolorifica relativamente intensiva può essere mantenuta a casa usando formulazioni orali di farmaci antinfiammatori non steroidei, morfina, tramadolo e gabapentina. Osservazioni mirate da parte del proprietario e controlli regolari potranno permet-

tere di interrompere progressivamente la terapia analgesica.
Infine, se l'analgesia epidurale toracica non è una procedura comune, l'alternativa di somministrare pre- e post-operativamente un singolo bolo di un oppioide idrofilico (morfina) nello spazio epidurale a livello lombo-sacrale si è rilevata clinicamente rilevante nell'aumentare l'analgesia, se comparata alla somministrazione sistemica, ed è facilmente realizzabile.[5,23-25] L'esecuzione di una tecnica combinata spinale-epidurale (CSE), costituita dalla combinazione di un bolo pre-operatorio intratecale (spinale) di fentanil e bupivacaina associato alla somministrazione di morfina e bupivacaina attraverso un catetere epidurale nella fase peri- e post-operatoria, è stata descritta con successo in un cane garantendo analgesia efficace.[12]
L'associazione nel pre-operatorio di antinfiammatori non steroidei, di oppiodi per via sistemica, blocchi dei nervi intercostali e analgesia epidurale, nel peri-operatorio di un'anestesia generale, oppioidi per via sistemica ed eventualmente un' analgesia accessoria per via endovenosa (ketamina e/o lidocaina), e nel post-operatorio un'analgesia intrapleurica, un'analgesia epidurale ripetuta e oppiodi per via sistemica tutti insieme forniscono un potente piano analgesico multimodale per la chirurgia toracica.[1] Una sindrome dolorifica post-operatoria persistente dovrebbe essere trattata con farmaci antinfiammatori non steroidei, oppioidi, tramadolo, gabapentina ed eventualmente ketamina in relazione ai sintomi e alla collaborazione del proprietario.

Bibliografia

1. Pascoe PJ. Thoracic surgery In: Seymour C, Duke T (Eds.): BSAVA Manual of Canine and Feline Anaesthesia and Analgesia. 2nd ed. Gloucester. British Small Animal Veterinary Association. (2007), pp230-243
2. Walsh PJ, Remedios AM, Ferguson JF, et al. Thoracoscopic versus open partial pericardectomy in dogs: comparison of postoperative pain and morbidity. Vet Surg 1999;28:472-479
3. Wetmore LA, Glowaski MM. Epidural analgesia in veterinary critical care. Clin Tech Small Anim Pract 2000;15:177-188
4. Schwarte LA, Picker O, Hohne C, et al. Effects of thoracic epidural anaesthesia on microvascular gastric mucosal oxygenation in physiological and compromised circulatory conditions in dogs. Br J Anaesth 2004;93:552-559
5. Kahn L, Baxter FJ, Dauphin A, et al. A comparison of thoracic and lumbar epidural techniques for post-thoracoabdominal esophagectomy analgesia. Can J Anaesth 1999;46:415-422
6. Feldman HS, Covino BG. Comparative motor-blocking effects of bupivacaine and ropivacaine, a new amino amide local anesthetic, in the rat and dog. Anesth Analg 1988;67:1047-1052
7. Feldman HS, Dvoskin S, Arthur GR, et al. Antinociceptive and motor-blocking efficacy of ropivacaine and bupivacaine after epidural administration in the dog. Reg Anesth 1996;21:318-326
8. Feldman HS, Dvoskin S, Halldin MH, et al. Comparative local anesthetic efficacy and pharmacokinetics of epidurally administered ropivacaine and bupivacaine in the sheep. Reg Anesth 1997;22:451-460
9. Skarda RT, Muir WW 3rd. Analgesic, behavioral, and hemodynamic and respiratory effects of midsacral subarachnoidally administered ropivacaine hydrochloride in mares. Vet Anaesth Analg 2003;30:37-50
10. Almeida TF, Fantoni DT, Mastrocinque S, et al. Epidural anesthesia with bupivacaine, bupivacaine and fentanyl, or bupivacaine and sufentanil during intravenous administration of propofol for ovariohysterectomy in dogs. J Am Vet Med Assoc 2007;230:45-51
11. Naganobu K, Maeda N, Miyamoto T, et al. Cardiorespiratory effects of epidural administration of morphine and fentanyl in dogs anesthetized with sevoflurane. J Am Vet Med Assoc 2004;224:67-70
12. Novello L, Corletto F. Combined spinal-epidural anesthesia in a dog. Vet Surg 2006;35:191-197
13. Berg RJ, Orton EC. Pulmonary function in dogs after intercostal thoracotomy: comparison of morphine, oxymorphone, and selective intercostal nerve block. Am J Vet Res 1986;47:471-474
14. Flecknell PA, Kirk AJ, Liles JH, et al. Post-operative analgesia following thoracotomy in the dog: an evaluation of the effects of bupivacaine intercostal nerve block and nalbuphine on respiratory function. Lab Anim 1991;25:319-324
15. Conzemius MG, Brockman DJ, King LG, et al. Analgesia in dogs after intercostal thoracotomy: a clinical trial comparing intravenous buprenorphine and interpleural bupivacaine. Vet Surg 1994;23:291-298
16. Thompson SE, Johnson JM. Analgesia in dogs after intercostal thoracotomy. A comparison of morphine, selective intercostal nerve block, and interpleural regional analgesia with bupivacaine. Vet Surg 1991;20:73-77
17. Dhokarikar P, Caywood DD, Stobie D, et al. Effects of intramuscular or interpleural administration of morphine and interpleural administration of bupivacaine on pulmonary function in dogs that have undergone median sternotomy. Am J Vet Res 1996;57:375-380
18. Guedes AG, Papich MG, Rude EP, et al. Pharmacokinetics and physiological effects of two intravenous infusion rates of morphine in conscious dogs. J Vet Pharmacol Ther 2007;30:224-233
19. Lucas AN, Firth AM, Anderson GA, et al. Comparison of the effects of morphine administered by constant-rate intravenous infusion or intermittent intramuscular injection in dogs. J Am Vet Med Assoc 2001;218:884-891
20. Muir WW, 3rd, Wiese AJ, March PA. Effects of morphine, lidocaine, ketamine, and morphine-lidocaine-ketamine drug combination on minimum alveolar concentration in dogs anesthetized with isoflurane. Am J Vet Res 2003;64:1155-1160
21. Solano AM, Pypendop BH, Boscan PL, et al. Effect of intravenous administration of ketamine on the minimum alveolar concentration of isoflurane in anesthetized dogs. Am J Vet Res 2006;67:21-25
22. Morton CM, Reid J, Scott EM, et al. Application of a scal-

ing model to establish and validate an interval level pain scale for assessment of acute pain in dogs. Am J Vet Res 2005;66:2154-2166
23. Popilskis S, Kohn D, Sanchez JA, et al. Epidural vs. intramuscular oxymorphone analgesia after thoracotomy in dogs. Vet Surg 1991;20:462-467
24. Dauphin A, Lubanska-Hubert E, Young JE, et al. Comparative study of continuous extrapleural intercostal nerve block and lumbar epidural morphine in post-thoracotomy pain. Can J Surg 1997;40:431-436
25. Pascoe PJ, Dyson DH. Analgesia after lateral thoracotomy in dogs. Epidural morphine vs. intercostal bupivacaine. Vet Surg 1993;22:141-147