The Veterinary Journal 220 (2017) 7–16

Contents lists available at ScienceDirect

The Veterinary Journal

journal homepage: www.elsevier.com/locate/tvjl

Proportion recovery and times to ambulation for non-ambulatory dogs with thoracolumbar disc extrusions treated with hemilaminectomy or conservative treatment: A systematic review and meta-analysis of case-series studies

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ARTICLE INFO

Article history:
Accepted 14 December 2016

Keywords:
Intervertebral disc disease
Neurological
Spinal

ABSTRACT

Thoracolumbar intervertebral disc extrusion is a common cause of spinal cord dysfunction in dogs. Peer-reviewed studies reporting treatment of predominantly chondrodystrophic dogs with disc extrusion with loss of ambulation with either hemilaminectomy or conservative treatment (rest, analgesics and anti-inflammatories) were evaluated in a systematic review of the literature.

Generally, the level of evidence available was low with no controlled studies and only case series available. In the meta-analysis, there was a clear trend to a greater proportion of dogs recovering and returning faster to ambulation for dogs treated with hemilaminectomy than for conservatively treated dogs. The mean proportions that recovered for neurological grades 3, 4 and 5 were 93, 93 and 61% for those treated with hemilaminectomy, and 79, 62 and 10% for those treated conservatively (Grade 3 – non-ambulatory paraparetic dogs; grade 4 – paraplegic dogs with intact deep pain perception; grade 5 – paraplegic dogs without intact deep pain perception). Due to the use of case series, these results represent between-study comparisons, thereby increasing the risk of selection bias and other biases. Data presented in this review support the current recommendations for surgical management of non-ambulatory dogs with disc-extrusion, but controlled clinical studies comparing outcomes are necessary to confirm these findings.

Introduction

Extrusion of thoracolumbar intervertebral discs is the most common cause of spinal cord dysfunction in dogs (Bray and Burbidge, 1998). Affected dogs are typically chondrodystrophic and aged between 3 and 6 years at presentation, although the condition can also occur in larger breeds. Compression of the spinal cord by extruded material, and by haematoma formation, produces clinical signs ranging from pain to paralysis (Besalti et al., 2005). However, there is no direct correlation between the degree of compression of the spinal cord and the severity of clinical signs. Sukhiani et al. (1996) reported substantial spinal cord compression in 25 dogs with back pain but no neurological deficits, whereas two other studies have reported significant neurological deficits despite only slight or non-compressive thoracolumbar disc extrusions, with the majority of dogs being non-ambulatory (De Risio et al., 2009; McKee et al., 2010).

The primary aim of surgery in dogs with thoracolumbar intervertebral disc extrusion is to remove the compressive disc material from around the spinal cord and prevent further local extrusion. Surgical procedures include fenestration, hemilaminectomy, mini-hemilaminectomy, pediculectomy and dorsal laminectomy. In a study by McKee (1992), hemilaminectomy was superior to dorsal laminectomy. Hemilaminectomy has been reported to have several advantages over dorsal laminectomy (McKee, 1992; Muir et al., 1995), including improved access to extruded material, easy access for local fenestration, greater biomechanical stability, and less effect on discal pressure. Reported proportion of dogs recovering with surgical management varies from 85 to 100% for non-ambulatory paraparetic dogs and from 73 to 100% for paraplegic dogs with intact deep perception (McKee, 1992; Scott, 1997; Necas, 1999; Ito et al., 2005; Kazakos et al., 2005; Aikawa et al., 2012).

Conservative treatment utilises rest, analgesia and anti-inflammatory medications (Sharp and Wheeler, 2005), although some recent reports also include acupuncture (Janssens and Prins, 1989; Hayashi et al., 2007; Han et al., 2010). Steffen et al. (2014) reported that in a conservatively managed French bulldog, disc extrusion volume on MRI decreased by 69% after 5 weeks and

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http://dx.doi.org/10.1016/j.tvjl.2016.12.008
1090-0233/

Table 1
Search strategy for the electronic databases in Ovid. The wildcard symbol '?' substitutes for one character or none, whereas the truncation symbol '*' substitutes for strings of zero or more characters.

Search no.	Strategy
1	dog? OR canine
2	disc OR disk OR extrusion OR protrusion OR neurosurg*
3	1 AND 2
4	decomp* OR surg* OR hemilam* OR laminec* OR facetec* OR foramino* OR corpec*
5	conservative treatment OR rest OR nonsurgical OR non-surgical OR cage rest OR medical OR no treatment
6	4 OR 5
7	3 AND 6

Table 2
Neurological grading system for this review. Non-ambulatory dogs are graded 3–5 depending on the severity of clinical signs (Scott, 1997). Individual study definitions of neurological grade were converted to the appropriate grade shown below to facilitate comparison between studies, using the definitions and descriptions given within each study.

Grade	Clinical signs
5	Paraplegia with loss of deep pain perception
4	Paraplegia with intact deep pain perception in at least one limb
3	Non-ambulatory paraparesis
2	Ambulatory paraparesis
1	Thoracolumbar pain with no neurological deficits
0	Normal

speculated that this phenomenon might explain successful outcomes in dogs treated conservatively. Conservatively managed humans with thoracolumbar disc extrusions showed similar reductions in the volume of extruded disc material over time (Maigne et al., 1992; Benson et al., 2010). The reported proportion of dogs recovering with conservative treatment varies considerably, ranging from 56 to 100% for non-ambulatory paraparetic dogs, and from 50 to 67% for paraplegic dogs with intact deep pain perception (Davies and Sharp, 1983; Levine et al., 2007; Han et al., 2010).

The evidence supporting the appropriate management of non-ambulatory dogs (i.e., surgical vs. conservative) is low grade and not based on controlled clinical trials. Since anaesthesia and surgery are not without some inherent risk, clinicians require reliable evidence to recommend particular courses of treatment, especially since surgical delay might impact subsequent recovery (Ferreira et al., 2002).

Our study used a systematic review and meta-analytic approach to answer the following clinical question: '*In non-ambulatory chondrodystrophic dogs with thoracolumbar disc extrusion, does hemilaminectomy increase the proportion of dogs that recover and decrease the time to ambulation, compared with conservative treatment?*'.

Materials and methods

A review protocol including search strategy and inclusion and exclusion criteria for the screening processes was defined prior to starting this review.

Inclusion and exclusion criteria

All studies which reported treatment of thoracolumbar disc extrusion by hemilaminectomy or conservative treatment were considered. Language was restricted to English, and no limitations were placed on date. Studies were restricted to those in which at least 50% of the dogs were chondrodystrophic, without limitations on age or gender. All dogs had to be non-ambulatory prior to treatment.

Studies, or individual dogs within studies, were excluded if treated with a decompressive surgery other than hemilaminectomy (surgical group) or with non-surgical modalities other than analgesics, anti-inflammatories and rest (conservative treatment group). Studies, or individual dogs within studies, were excluded if there were insufficient data regarding pre- and post-treatment neurological status, or if the total number of dogs treated (across all grades) was <15. Studies which were not peer-reviewed, based on publisher's webpage or the article's cover-page, were excluded.

Studies were excluded entirely or partly from the review process if they did not report the number of treated dogs that recovered to an acceptable neurological status, defined as the presence of deep pain perception and the ability to walk (with or without residual ataxia), or the length of time from the initiation of treatment until the dog recovered the ability to walk without assistance.

Follow-up time postoperatively had to be recorded, with adequate assessment of status by direct examination, detailed questionnaire or telephone consultation, and reported in sufficient detail for data extraction.

Search methods

Studies were identified by searching electronic databases (Medline and CAB Abstracts via Ovid) and manual screening of reference lists from retrieved articles. The search was carried out during November 2015 using the terms provided in Table 1, with search results restricted to English language articles.

Titles and abstracts of retrieved articles were reviewed by one author as an initial screening, using the inclusion criteria above. The full text of all potentially relevant studies was then assessed using the stated exclusion criteria.

Relevant studies were assessed for the risk of study bias using the methodological index for non-randomised studies (MINORS) to assess the methodological quality of the studies, as described by Slim et al. (2003).

Data extraction

Both authors independently extracted the data, including signalment, number of dogs treated, pre-operative neurological status, number that recovered to acceptable neurological status, time to recovery of ability to walk independently. The proportion that recovered was defined as the proportion of dogs treated that recovered to an acceptable neurological status. A post-hoc decision was made to exclude dogs that died or were euthanased prior to the start of treatment, but include dogs that died or were euthanased (irrespective of cause) during the follow-up period as treatment failures. Any discrepancies between the two data extractions were resolved by discussion and consensus.

When necessary, week and month data for time to recovery to an acceptable neurological status were converted to days (using 1 month = 365/12 days). Age data were extracted from the text or calculated from frequency data (Anderson et al., 1991; Olby et al., 2003; Levine et al., 2007; Han et al., 2010). Duration of clinical signs prior to presentation was extracted from the text or calculated from partial data or charts (Davies and Sharp, 1983; Ito et al., 2005; Hayashi et al., 2007; Levine et al., 2007). Duration of clinical signs data was standardised to days as above.

Several different neurological grading systems were found in the included studies. For consistency, grades for non-ambulatory dogs were converted post-hoc to a standard scale using published criteria (Scott, 1997; Table 2); the definition of neurological grade from each study served as the basis for conversion. Where studies employed additional sub-divisions of clinical severity, these were combined as appropriate.

Outcome measures from individual studies for each pre-treatment neurological grade were combined where possible using a DerSimonian–Laird random-effects model in Open Meta-Analysis.[1] Subgroup analysis was performed for the surgical and conservative treatment groups. Raw proportional data for meta-analysis of recovery to an acceptable neurological status were logit transformed for analysis. Proportions of zero or one were automatically adjusted to permit transformation to avoid infinite values, and results were back-transformed for presentation. Heterogeneity between studies was tested using the I^2 quantity (Higgins et al., 2003).

Results

Twenty studies were identified for inclusion in this review. The initial search of Medline and CAB Abstracts yielded 1434 citations. Two additional studies were identified through reference searches. After removing duplicates, 1046 citations remained. Screening of titles and abstracts resulted in 1002 records being discarded as clearly not meeting inclusion criteria. The full text of 44 articles was examined in more detail, resulting in 20 studies that met the inclusion criteria for this review (Fig. 1). The studies excluded at the full text stage are listed in Appendix S1 with reasons for their exclusion. Of the included studies, 16 were retrospective case-series and four were prospective case-series (Bush et al., 2007; Hayashi et al., 2007; Muguet-Chanoit et al., 2012; Roach et al., 2012), classified as level 4 evidence using Oxford Centre for Evidence Based Medicine criteria. Using these criteria, evidence levels range from

[1] See: Journal of Statistical Software. http://dx.doi.org/10.18637/jss.v049.i05 (Accessed 7 December 2016).

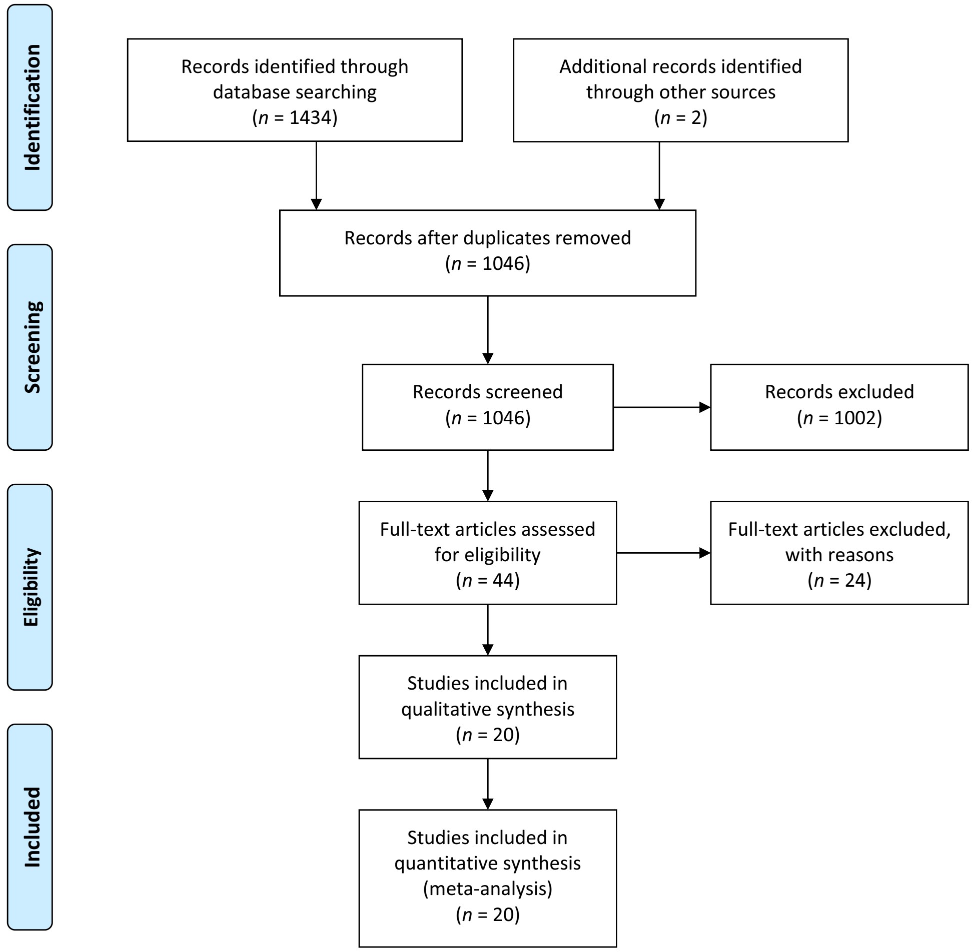

Fig. 1. PRISMA flow diagram (Moher et al, 2009) of study selection. Excluded studies are listed in Appendix S1.

1 to 5, where level 1 represents the highest evidentiary value and level 5 represents the lowest.[2]

Summary data for the included studies are presented in Table 3. In three studies (McKee, 1992; Olby et al., 2003; Bush et al., 2007), only mean time to recovery and range were reported, and the standard deviation was estimated from published formulae using the range and the number of recovered dogs, as described by Wan et al. (2014). Two studies (Necas, 2000; Aikawa et al., 2012) sub-divided neurological grades, and weighted pooled means and standard deviations were derived from the published data.

For the surgical group, in addition to hemilaminectomy at the site of compression, four studies reported additional fenestration of adjacent discs in all cases, one study reported additional fenestration in some cases, four studies did not perform additional fenestration in any cases, and seven studies did not report whether or not fenestration was performed. Dogs were additionally treated with perioperative analgesia and with glucocorticoids (methylprednisolone succinate, prednisolone or dexamethasone) or non-steroidal anti-inflammatory drugs.

Dogs in the conservative treatment group received prednisolone in all cases (two studies), glucocorticoids in most cases (one study) and treatment type was not directly reported in the fourth study.

[2] See: OECBM Levels of evidence. http://www.cebm.net/index.aspx?o=5653 (Accessed 7 December 2016).

Four studies (McKee, 1992; Ruddle et al., 2006; Bush et al., 2007; Hayashi et al., 2007) used a neurological scoring system which prevented separation of some or all outcome data for dogs with neurological grades 3 and 4.

Underlying population data for the included studies are summarised in Table 4.

Meta-analysis

Meta-analysis of the extracted data for recovery to an acceptable neurological status was performed for studies in which appropriate data were available (Fig. 2), with sub-grouping of surgical and conservative treatment groups. Fewer data were available to enable meta-analysis for time to recovery of independent ambulation (Fig. 3) and sub-group analysis was only possible for neurological grade 4.

For initial neurological grades 3, 4 and 5, a greater proportion of dogs recovered following hemilaminectomy than conservative treatment. For grades 4 and 5, these differences were statistically significant ($P < 0.01$), based on non-overlap of the 95% confidence intervals (CI; Knol et al., 2011). For grade 3, the 95% CIs overlapped. Based on the standard errors (0.24 and 1.35) and number of studies (eight and two) in the analysis, a ratio of the standard deviations (rho) of 2.8 was calculated. According to Knol et al. (2011), for rho = 2.8, CI of 85% will not overlap at $P < 0.05$; recalculated CIs were 0.91–0.95 and 0.35–0.96 after hemilaminectomy and

Table 3
Summary data for the 20 included studies. Primary outcome data for the studies meeting the inclusion criteria are shown. Studies are listed by first author and date.

	Grade[a]	N[b]	N[c]	Proportion recovered[d] (%)	Time[e] (days)	Range[f] (days)	Diagnostic methods[g]
Hemilaminectomy							
Aikawa et al. (2012)	3	184	171	93	8 ± 8		M, MRI
Bush et al. (2007)[g]	3	25	25	100			M
Kazakos et al. (2005)	3	6	6	100	15 ± 23		M
McKee (1992)	3	23	22	96			M
Necas (1999)	3	68	68	100			M
Necas (2000)	3				11 ± 7		M
Roach et al. (2012)	3	13	13	100			CT
Scott (1997)	3	13	11	85		3–14	M
Srugo et al. (2011)[g]	3	9	9	100		5-->100	M
Aikawa et al. (2012)[h]	4	161	158	98	11 ± 12		M, MRI
Bush et al. (2007)[g]	4	26	26	100			M
Ferreira et al. (2002)	4	71	61	86	11 ± 8		M
Ito et al. (2005)	4	48	44	92	45[i]	7–180	MRI
Kazakos et al. (2005)	4	11	8	73	27 ± 16		M
McKee (1992)	4	5	5	100			M
Necas (1999)	4	167	159	95			M
Necas (2000)[h]	4				16 ± 12		M
Roach et al. (2012)	4	15	15	100			CT
Scott (1997)	4	15	14	93		7–28	M
Srugo et al. (2011)[g]	4	29	29	100		5-->100	M
Aikawa et al. (2012)	5	211	110	52	21 ± 22		M, MRI
Anderson et al. (1991)	5	30	25	83	47 ± 46		M
Ito et al. (2005)	5	28	18	30[i]		14–270	MRI
Kazakos et al. (2005)	5	8	4	50	42 ± 23		M
Laitinen and Puerto (2005)	5	39	17	44			M
McKee (1992)	5	2	0	0			M
Muguet-Chanoit et al. (2012)	5	31	18	58		<140[i]	M, MRI, CT
Necas (1999)	5	36	29	81			M
Necas (2000)	5				39 ± 34		M
Olby et al. (2003)[j]	5	64	37	57	53 ± 58	<7–252	M
Roach et al. (2012)	5	2	2	100			CT
Ruddle et al. (2006)	5	32	22	69		<84	M
Scott (1997)	5	3	2	67		42–56	M
Srugo et al. (2011)	5	16	9	56		5-->100	M
Bush et al. (2007)[j]	3 + 4	51	51	100	7 ± 8	1–35	M
McKee (1992)[j]	3 + 4	28	27	96	11 ± 10	3–42	M
Ruddle et al. (2006)	3 + 4	218	200	92			M
Conservative							
Davies and Sharp (1983)	3	10	10	100	63		N, R
Levine et al. (2007)	3	23	13	57			N
Davies and Sharp (1983)	4	6	3	50	84		N, R
Han et al. (2010)	4	37	25	68	19 ± 4		N, MRI
Levine et al. (2007)	4	12	6	50			N
Davies and Sharp (1983)	5	14	1	7			N, R
Hayashi et al. (2007)	5	8	1	13	18		N, R
Levine et al. (2007)	5	3	0	0			N
Hayashi et al. (2007)	3 + 4	9	6	67	21		N, R

M, myelography; N, neurological examination; R, radiography.
[a] The grade corresponds to the system defined for this review – alternative systems used in other studies were converted to this.
[b] *N*, total number of dogs that entered treatment.
[c] *n*, number of dogs that recovered to acceptable neurological status.
[d] Proportion recovered is calculated as n/N and presented as a percentage rounded to the nearest whole number.
[e] Time (mean [unless noted otherwise] ± standard deviation where available) from start of treatment to recovery of independent ambulation as defined by each study.
[f] Range in days for time to recovery of independent ambulation. One study population had proportion that recovered and times to ambulation presented separately in two articles (Necas, 1999, 2000).
[g] Recovery data were published jointly for grades 3 and 4, but are presented separately here since proportion that recovered was 100% for both grades.
[h] Neurological grades were sub-divided further than those used in this review: weighted pooled data are presented.
[i] Upper limit for 15 of 18 dogs.
[j] Standard deviations were estimated from range data and number of recovered dogs using published formulae (Wan et al., 2014).

conservative treatment respectively, indicating there was not a significant difference between groups ($P > 0.05$). The proportions of dogs that recovered in case-series describing hemilaminectomy for grades 3 and 4 were similar at 93% (90–96%) and 93% (88–96%) and were higher than the proportions of dogs that recovered in case-series describing conservative treatment for grades 3 and grades 4 (79%, 95% CI: 21–98%; and 62%, 95% CI: 48–74%), respectively. In dogs without deep pain perception (grade 5), a greater proportion of dogs recovered in case-series describing hemilaminectomy (61%, 95% CI: 53–68%) than in those describing conservative treatment (10%, 95% CI: 3–29%). Heterogeneity was high for the grade 3 conservative treatment group, and moderate for the grade 4 and grade 5 surgical groups.

As initial neurological grade increased from 3 to 5 in case-series describing hemilaminectomy, time to recovery to acceptable neurological function increased from a mean of 10 days (grade 3) to 15 days (grade 4) and 38 days (grade 5). For both grades 3 and 4, these estimates were potentially skewed upwards by one outlier

Table 4
Population data for the included studies. Studies are listed by first author.

	Age[a]		Duration of clinical signs[a]		Male[b]	Female[b]	Follow-up[c]	Breeds[d]
	Mean	Range	Mean	Range				
Hemilaminectomy								
Aikawa et al. (2012)[e]	6.0*	1–15	3*	0–304	367 (133)	222 (109)	35* (1–123)	Dachshund (81%), Pembroke Welsh corgi (3%), French bulldog (3%), Shih Tzu (2%), beagle (2%), Cocker spaniel, Pekingese, toy poodle, Bassett hound, crossbreeds, non-chondrodystrophic (5%)
Anderson et al. (1991)	4.8	2–15	NR	0–5	NR	NR	17 (1–48)	Dachshund (28%), mixed breed (16%), Cocker spaniel (9%), Lhasa Apso (6%), Cockapoo (6%), poodle (6%), Chihuahua, Labrador retriever, Miniature poodle, Coton de Tulear, toy poodle, Shih Tzu, Cairn terrier, Dalmatian, terrier
Bush et al. (2007)	6.3	3–13	NR	NR	4 (23)	2 (22)	4 (EP)	Dachshund (47%), mixed breed (10%), Shih Tzu (8%), beagle (6%), Bichon Frise (6%), other pure breeds
Ferreira et al. (2002)	5.3	3–10	6.7	1–60	43	28	29 (NR)	Cocker spaniel (25%), miniature poodle (17%), Pekingese (14%), dachshund (14%), Shih Tzu (3%), Bichon Frise, Basset hound, Lhasa Apso, Cavalier King Charles spaniel, French bulldog, American Cocker spaniel, mixed breed (18%), German shepherd dog (2%)
Ito et al. (2005)[f]	5.7	2–14	8	1–30	31 (14)	24 (8)	NR (12-NR)	Miniature dachshund (79%), Shih Tzu (4%), American Cocker spaniel (3%), Shetland sheepdog (3%), beagle, Cavalier King Charles spaniel, Standard dachshund, toy poodle, pug, Maltese, Siberian husky, Welsh Corgi, mixed breed
Kazakos et al. (2005)[e]	NR	3–10	7	1–20	13	17	6 (3–24)	Pekingese (20%), Mongrel (37%), Cocker spaniel (7%), poodle (17%), poodle cross (10%), beagle cross (7%), Yorkshire terrier (3%)
Laitinen and Puerto (2005)[g]	5.3	3–14	NR	NR	18	28	13* (0–51)	Dachshund (44%), beagle (11%), Lhasa Apso (7%), other chondrodystrophic (11%), non-chondrodystrophic (7%), mixed breed (22%)
McKee (1992)[h]	5.8	2–11	4	1–28	33	27	30 (NR)	Chondrodystrophic (78%)
Muguet-Chanoit et al. (2012)[i]	4.5	2–7	NR	NR	2 (18)	3 (13)	NR (7–36)	Dachshund (64%), beagle (8%), Pekinese (6%), Chihuahua (6%), Lhasa Apso, Corgi, Shi-Tzu, miniature poodle, American Staffordshire terrier, mixed breed
Necas (1999)[e]	6.8	2–13	NR	NR	172	128	NR (9–51)	Dachshund (71%), Mongrel (9%), Cocker spaniel (3%), Miniature Schnauzer (2%), poodle (2%), French bulldog (2%), Lhasa Apso (1%), Basset hound (1%), American Cocker spaniel (1%), Shih Tzu (1%)
Necas (2000)[e]	6.8	2–13	NR	NR	172	128	NR (9–51)	Dachshund (71%), Mongrel (9%), Cocker spaniel (3%), Miniature Schnauzer (2%), poodle (2%), French bulldog (2%), Lhasa Apso (1%), Basset hound (1%), American Cocker spaniel (1%), Shih Tzu (1%)
Olby et al. (2003)[j]	5.1	2–11	NR	NR	13 (21)	6 (30)	21 (6–84)	Dachshund (66%), Cocker spaniel (6%), mixed breed (6%), Basset hound (4%), beagle (3%), Pekingese (3%), Jack Russell terrier (3%), pug, Shih Tzu, Bichon Frise, Rottweiler, German shepherd dog, Labrador retriever
Roach et al. (2012)[e]	5.1	2–10	NR	0–21	3 (15)	2 (20)	19 (3–24)	Dachshund (68%), Lhasa Apso (8%), Pekingese (8%), mixed breed (8%), Basset hound, Cocker spaniel, Shih Tzu, Welsh corgi
Ruddle et al. (2006)	6.0	1–14	NR	NR	24 (116)	8 (102)	3 (EP)	Dachshund (56%), beagle (8%), Basset hound (NR), Pekingese (NR), Shih Tzu (NR), other (NR)
Scott (1997)[e]	6.5	2–14	NR	NR	26	14	34 (12–72)	Dachshund (45%), mixed breed (8%), Pekingese (5%), Basset hound (5%), Jack Russell terrier (5%), Shih Tzu (5%), Cocker spaniel (5%), Cavalier King Charles spaniel, Chihuahua, Pembroke Corgi, beagle, Dandie Dinmont, Sealyham, Yorkshire terrier, German shepherd dog, American Cocker spaniel (all 3%)
Srugo et al. (2011)	4.0 *	1–11	0.75	0–7	23 (6)	9 (16)	NR (3–12)	Dachshund (24%), Pekingese (22%), French bulldog (15%), Cocker spaniel, Shih Tzu, Maltese, poodle, mixed breed (22%)
Conservative								
Davies and Sharp (1983)[k]	6.1		12		NR	NR	NR (12–NR)	Chondrodystrophic (86%)
Han et al. (2010)	4	NR	NR	NR	19	18	29 (12–48)	Pekingese (30%), Shih Tzu (19%), Cocker spaniel (16%), mixed breed (11%), Dachshund (8%), toy poodle (5%), Yorkshire terrier (5%), Maltese (5%)
Hayashi et al. (2007)[e]	4.8	NR	19	NR	14	10	1,17 (NR)	Dachshund (67%), Cocker spaniel (17%), poodle (13%), Pekingese (4%)
Levine et al. (2007)[e]	6.2	NR	11	NR	NR	NR	39 (5–85)	Dachshund (39%), mixed breed (10%), poodle (5%), beagle (5%), Lhasa Apso (4%), Cocker spaniel (4%), Miniature Schnauzer (4%), Chihuahua (3%), Pekingese (2%), Shih Tzu (2%), 35 other breeds

EP, study end-point; NR, not reported or not extractable from reported data.
* Value is median instead of mean.
[a] Where available, mean age and range in years, and mean duration of clinical signs and range prior to presentation in days are shown. Where necessary, values were converted to the formats shown using 1 month = 30.4 days. Day values are rounded to the nearest whole value, and those under 0.5 (12 h) are given as 0.
[b] The numbers of male and female dogs are listed: when only one figure is supplied this refers to both intact and neutered animals, otherwise the figure outside parentheses refers to intact animals and that within parentheses refers to neutered animals.
[c] Follow-up time is given in months as mean (minimum–maximum).
[d] Breeds are listed along with their percentage contribution to the presenting population (when 2% or more). Due to the limitations in the available data, the population totals vary in some cases from those in Table 4. Reasons for deviations are noted in numbered footnotes.
[e] Presenting population included dogs with ambulatory neurological grades.
[f] One dog died before surgery.
[g] Seven dogs underwent dorsal laminectomy.
[h] Thirty dogs underwent dorsal laminectomy.
[i] Five dogs were lost to follow-up.
[j] Eight dogs were euthanased before surgery.
[k] Surgical population underwent fenestration only.

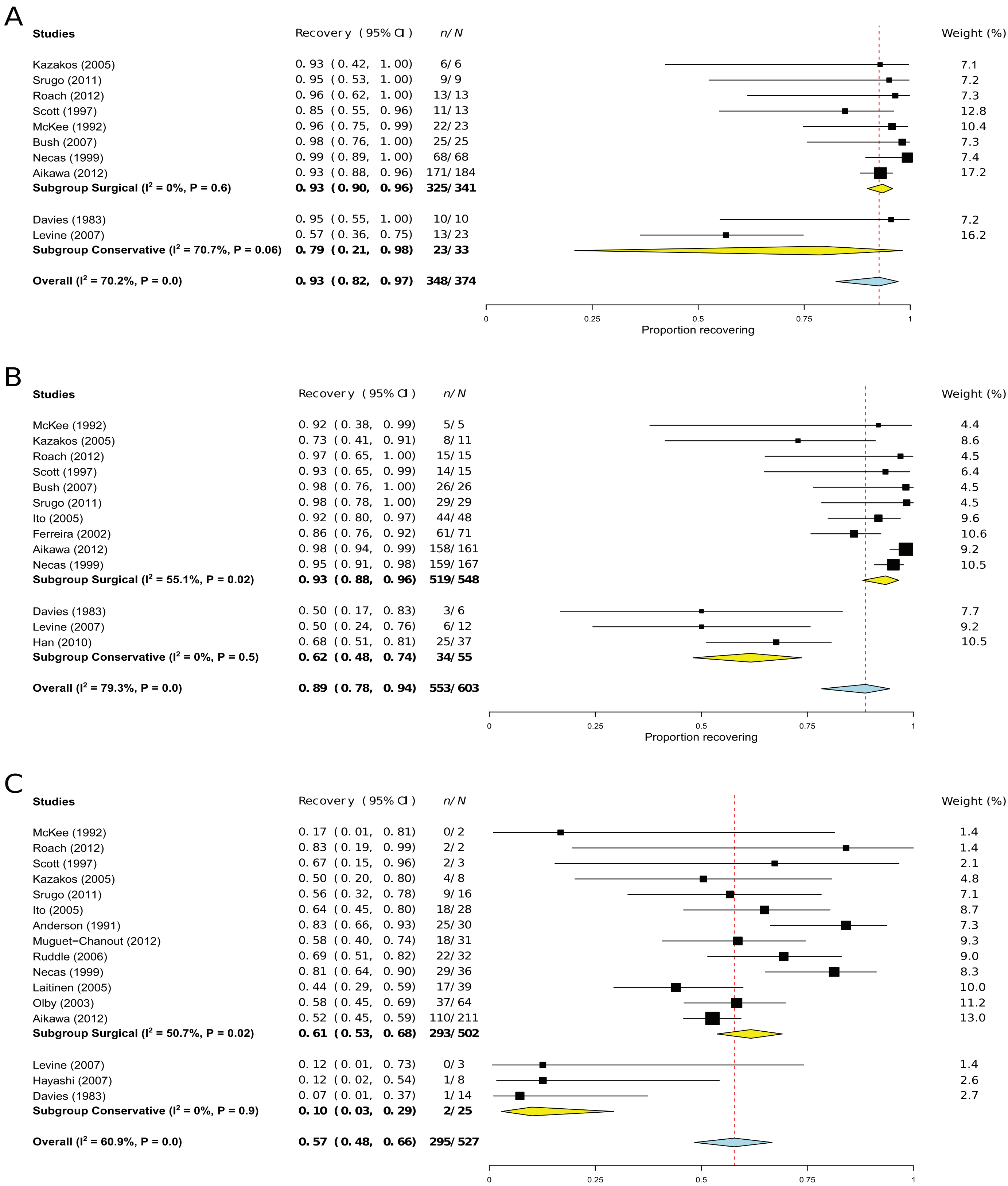

Fig. 2. Proportion of non-ambulatory dogs with thoracolumbar disc disease that recovered. Forest plots for dogs with neurological grades 3 (A), 4 (B) and 5 (C). Studies are identified by first author and date, and ordered by increasing study population. Logit transformation of data was used: back-transformed proportions of dogs that recovered with 95% confidence intervals (CI) for each study are shown. The number of dogs that recovered to acceptable neurological status as defined in the text is shown as *n*, and the total number of dogs entering treatment is shown as *N*. Square markers denote the point estimate for the proportion that recovered for each study, with size reflecting the relative study size (*N*); the bars represent the 95% CI for the point estimate. The diamonds represent summary data for proportion that recovered for each subgroup (surgical or conservative treatment) and overall recovery rates for each grade. The I^2 value reflects data heterogeneity across subgroups or all data. Weighting for each study in the random effects model is given on the right side of the forest plot.

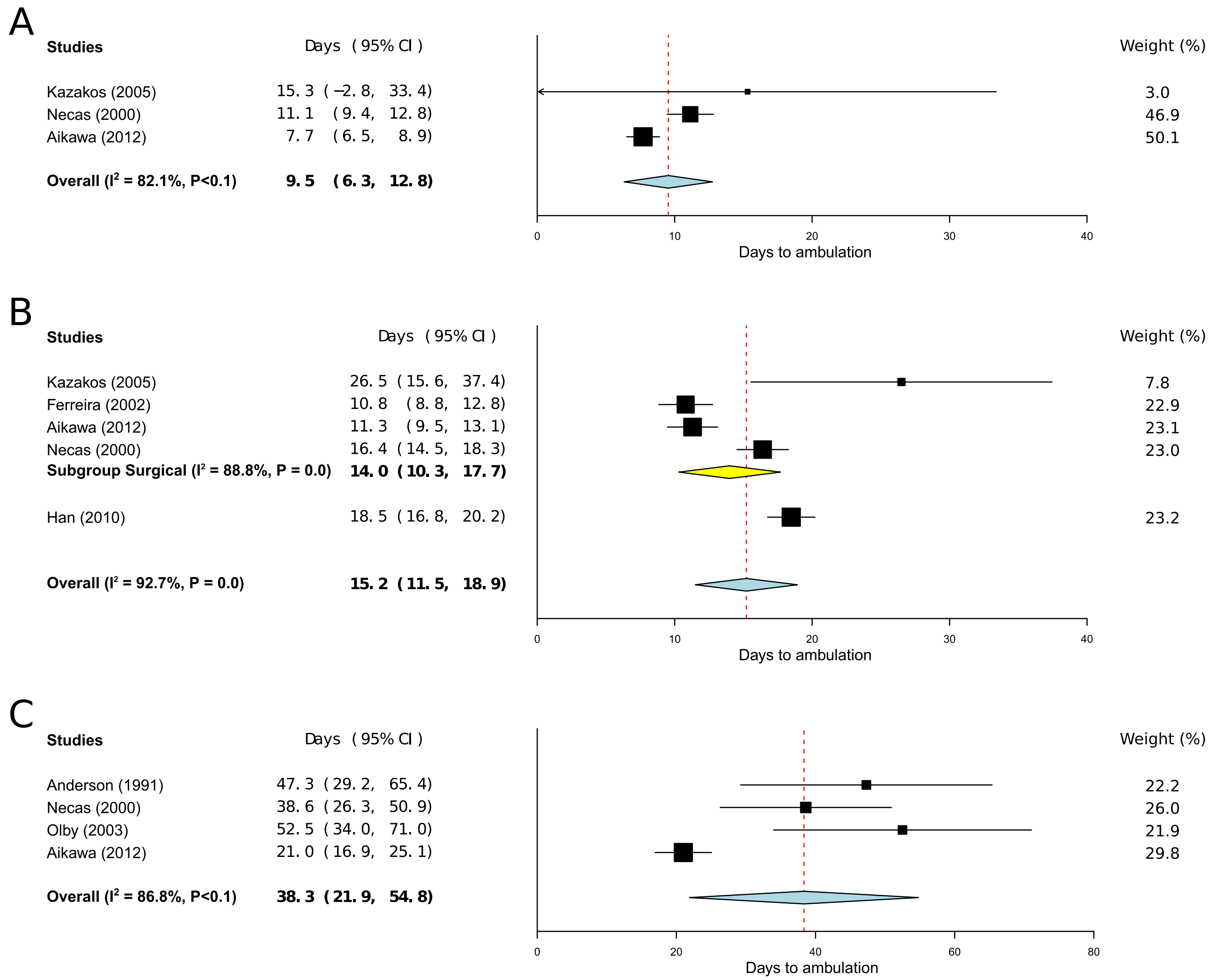

Fig. 3. Time to independent ambulation for non-ambulatory dogs with thoracolumbar disc disease. Forest plots for dogs with neurological grades 3 (A), 4 (B) and 5 (C). Studies are identified by first author and date, and ordered by increasing study population. Mean number of days and the 95% confidence interval (CI) for each study are shown. Square markers denote the point estimate for the proportion that recovered for each study, with size reflecting the relative study size (*N*); the bars represent the 95% CI for the point estimate. Diamonds represent summary data for times to ambulation. The I^2 value reflects data heterogeneity across subgroups or all data. Weighting for each study in the random effects model is given on the right side of the forest plot.

study. Since the study by Han et al. (2010) was the only conservative study to present standard deviations, only this study could be compared directly with those describing hemilaminectomy; this study reported a longer mean recovery period of 18.5 days for dogs with grade 4 neurological signs. Additionally, studies describing conservative treatment generated point estimates for mean recovery time of 63 days (grade 3), 84 days (grade 4) and 18 days (grade 5). Heterogeneity for time to recovery was high for surgical studies at all grades.

Bias assessment

A summary of the risk of bias assessment for the included studies is given in Table 5. No studies made prospective calculations of study size, and only four studies had a prospective design, which markedly impacted the total scores for each study. The surgical studies as a group had a mean MINORS score of 8.8 out of a possible score of 16, where 16 represents the best score; non-surgical studies had a mean MINORS score of 7.3.

Discussion

A large number of case series describing treatment-outcome after thoracolumbar disc extrusion exist, but the present study is the first systematic review to collect and compare the results. Despite the large number of publications available, relatively few met our inclusion criteria. No randomised controlled trials or cohort studies were available for analysis. The grades of evidence included in this review should, therefore, be considered low. In general, the results presented here suggest that hemilaminectomy for non-ambulatory thoracolumbar disc disease results in a higher proportion of recovered dogs and the time to ambulation is shorter compared to conservative treatment, supporting current recommendations for decompressive surgery for non-ambulatory dogs (Scott, 1997; Levine et al., 2007; Aikawa et al., 2012).

The two primary outcome measures (proportion of dogs that recovered and time to independent ambulation) selected for this study were chosen for their ease of definition and extraction. Other outcome measures of interest, such as sequential improvements in

Table 5
Risk of bias summary for included studies. The table is subdivided into surgical and conservative treatment papers, and each item is scored according to the MINORS grading system for non-comparative studies (Slim et al., 2003). The items are scored 0 (not reported), 1 (reported but inadequate) or 2 (reported and adequate). Studies are listed by first author and year.

	Aim[a]	Inclusion[b]	Design[c]	End-points[d]	Assessment[e]	Follow-up[f]	Loss to follow-up[g]	Study size[h]	Total[i]
Hemilaminectomy									
Anderson et al. (1991)	2	1	0	2	1	2	1	0	9
Aikawa et al. (2012)	2	1	0	2	1	2	2	0	10
Ferreira et al. (2002)	2	1	0	2	0	2	2	0	9
Bush et al. (2007)	2	0	0	2	1	2	1	0	8
Ito et al. (2005)	2	1	0	1	1	1	2	0	8
Kazakos et al. (2005)	2	2	0	2	0	2	0	0	8
Laitinen and Puerto (2005)	2	2	0	2	0	2	2	0	10
McKee (1992)	2	0	0	1	0	2	1	0	6
Muguet-Chanoit et al. (2012)	2	1	0	2	0	2	2	0	9
Necas (2000)	2	1	0	2	0	2	1	0	8
Necas (1999)	1	1	0	1	1	2	2	0	8
Olby et al. (2003)	2	1	0	2	0	2	2	0	9
Roach et al. (2012)	2	1	0	2	1	2	2	0	10
Ruddle et al. (2006)	2	1	0	1	0	1	1	0	6
Scott (1997)	1	1	0	1	0	2	2	0	7
Srugo et al. (2011)	2	0	0	2	2	2	1	0	9
Conservative									
Davies and Sharp (1983)	2	1	0	1	0	1	1	0	6
Han et al. (2010)	2	1	0	2	1	2	0	0	8
Hayashi et al. (2007)	1	2	2	1	1	1	0	0	8
Levine et al. (2007)	2	1	0	2	0	2	0	0	7

[a] A clearly stated study aim.
[b] Inclusion of consecutive dogs.
[c] Prospective collection of data.
[d] Endpoints appropriate to the aim of the study.
[e] Unbiased assessment of the study endpoints.
[f] Follow-up period appropriate to the aims of the study.
[g] Less than 5% loss to follow-up.
[h] Prospective calculation of the study size.
[i] The total score across all items is given in the last column as a guide to the overall methodological quality of the paper.

neurological grade or time to discharge, were not consistently reported. Mean proportions of dogs that recovered were consistently better for dogs managed surgically, but this result might be biased by several factors. Independent ambulation was selected as a primary outcome due to its relative ease of identification by both owners and clinicians. This helps minimise bias when follow-up was performed by telephone interviews or by questionnaires. Most studies in this review define independent ambulation as the dog being able to walk without assistance, while others define it as being able to take three steps without support, and finally some do not define it at all, which complicates comparisons. Additionally, time to ambulation is generally reported from the start of treatment, although dogs might have been non-ambulatory for varying periods prior to the definitive diagnosis and start of conservative treatment or surgical management. For example, in the study by Hayashi et al. (2007), the average time to enter the study was more than 10 days, and these data were not included in the studies by Levine et al. (2007) and Han et al. (2010). It is worth noting that time to independent ambulation does not necessarily equate to time to discharge, since many of these dogs could potentially be managed at home or on an out-patient basis once they established urinary continence.

Relatively few studies presented all the necessary data for subsequent meta-analysis, particularly with respect to time to ambulation for conservatively treated dogs, which limits the weight that can be attached to the estimates presented here.

Whereas two authors performed full text assessment and data extraction, only one author performed the initial screening of titles and abstracts, which presents a potential bias in study selection.

No high-quality studies were identified for inclusion in this review, which was restricted to case series. Classically, the focus of systematic reviews has been the randomised clinical trial, because randomisation is a powerful tool to control potential confounders (O'Neil et al., 2014). Medical healthcare systematic reviews have increasingly begun to include non-randomised studies, especially when randomised studies could be considered impractical, unethical, or not reflective of real-world settings (O'Neil et al., 2014). Results of reviews using randomised vs. non-randomised studies disagree significantly in 35% of cases, but the rigid exclusion of non-randomised or observational studies from systematic reviews might not be appropriate (Peinemann et al., 2013). Of the main reasons the Cochrane Centre has identified for using non-randomised studies in a Cochrane review, '*the provision of evidence of effects (benefit or harm) of interventions that cannot be randomised or which are extremely unlikely to be studied in randomised trials*' is of particular relevance to the review presented here.[3] A major problem with the use of case series as opposed to randomised or cohort studies is that considerable selection bias can occur between case-series studies, and therefore between the treatment groups being compared. Although similar breeds and ages of dogs were included in all studies where this information was available, the duration of clinical signs prior to presentation was generally greater in the conservative treatment group. Fewer studies and dogs were available for analysis in the conservative treatment group, and dogs in this group were less likely to have the presumptive diagnosis of disc extrusion confirmed with myelography, CT or MRI. According to Levine et al. (2007), it is likely that in a proportion of dogs where the diagnosis was made clinically, other conditions leading to myelopathy were present. In the absence of randomised allocation to treatment groups, it is possible that owners opting for conservative treatment were

[3] See: Chapter 13: Including non-randomized studies. In: Higgins, J.P.T. and Green, S. (Editors). Cochrane Handbook for Systematic Reviews of Interventions Version 5.1.0 (Updated March 2011) The Cochrane Collaboration. http://handbook.cochrane.org/chapter_13/13_including_non_randomized_studies.htm (Accessed 6 December 2016).

less committed to treatment, or that financial pressures result in euthanasia before clinical improvement could be observed due to the potentially prolonged recovery times with conservative treatment.

The evidence presented in this review is affected by multiple additional sources of bias. Many of the studies included were relatively small, detrimentally affecting the CIs of the reported proportion that recovered. In addition, some studies had greater variability in outcome compared to others. This might reflect differences in case selection, surgical experience and technique, learning effect, variations in neurological grading (both in definition and in application), and different anaesthetic and perioperative protocols. These sources of bias are the likely cause of the widely fluctuating heterogeneities seen in the meta-analysis. To compensate as far as possible for these potential confounding effects, we used a random effects model to estimate the means and CIs for the two primary outcome measures.

We limited the studies by language, which potentially could have excluded some relevant non-English language studies. For conditions with particular geographic prevalences, language limitations can lead to selection bias (Crowther et al., 2010), although we have no reason to suspect this in this review based on the population data in Table 4.

Studies were restricted to those reporting at least 15 dogs, based on three neurological grades per study with five dogs in each: for proportional comparisons, a sample size of five dogs per group allows an 80% difference to be detected at $P = 0.05$ with 80% power (Campbell et al., 1995). This could have introduced selection bias in our comparisons by focusing on results from larger clinics and hospitals, and might not, therefore, reflect results obtained in clinics with low caseloads. However, it can be argued that even this limit is set low from a statistical viewpoint.

We attempted to minimise bias by restricting the surgical intervention to hemilaminectomy and the conservative treatment to treatment primarily with rest and anti-inflammatory medication. Additional non-surgical techniques such as acupuncture or electro-acupuncture were excluded. However, even with the hemilaminectomy intervention group, there were differences in the surgical time taken for the hemilaminectomy and the use of disc fenestration at adjacent discs. It was not possible to control for these effects due to limitations on the available data.

To minimise bias due to any difference in the pathogenesis and management of disc extrusion in chondrodystrophic and non-chondrodystrophic dogs, we restricted studies to those predominantly consisting of chondrodystrophic dogs: although a few non-chondrodystrophic dogs were included, good results after hemilaminectomy in large breed paraplegic dogs with intact deep pain perception indicate that any potential bias due to variation in included breeds should be small (Cudia and Duval, 1997; Macias et al., 2002). Similar breeds and breed distributions were seen for most studies.

The majority of dogs in both treatment groups received glucocorticoids, although treatment regimens varied in terms of steroid used, dose and treatment length. One study in the non-surgical group reported that the administration of glucocorticoids negatively impacted outcome (Levine et al., 2007). However, two studies not included in this review (Davis and Brown, 2002; Olby et al., 2016) did not show any effect of glucocorticoids on recovery, the latter being a placebo-controlled, prospective, randomised study. This indicates that any potential bias due to glucocorticoid administration should be small. The use of physiotherapy is only mentioned in a few studies, so it is uncertain if physiotherapy given in some studies represents a potential bias.

Methodological bias was present in all studies to varying degrees. The retrospective nature of all but four studies and the lack of study size calculations resulted in marked down-scoring of all included studies. Results reported by Levine et al. (2007) were based on the use of self-administered client questionnaire follow-up, another potential bias.

Surgical studies that employed dorsal laminectomy were excluded from this review, even though there were several case series of comparable quality available in the published literature (Duval et al., 1996; Scott and McKee, 1999; Davis and Brown, 2002). Extruded nuclear material cannot be removed as efficiently in dorsal laminectomy as in a hemilaminectomy (McKee, 1992; Muir et al., 1995), and one study demonstrated that decompression by laminectomy alone was not sufficient to restore spinal cord function when an extradural mass greater than 4 mm was present (Doppman and Girton, 1976).

Conclusions

Based on grades of the available evidence, it was not possible to definitively answer the research question. Most studies in this systematic review were retrospective case-series, and higher quality studies are needed to establish the true effect of hemilaminectomy compared to conservative treatment. However, for non-ambulatory dogs with thoracolumbar disc disease, hemilaminectomy appeared to result in a greater proportion of recovered dogs than conservative treatment. For dogs with neurological grades 4 and 5, these differences were statistically significant ($P < 0.01$). These results support the current recommendations for decompressive surgery for non-ambulatory dogs. As initial neurological grade increased from 3 to 5, time to ambulation after hemilaminectomy increased from a mean of 10 days (grade 3) to 15 days (grade 4) and 38 days (grade 5).

Conflict of interest statement

None of the authors of this paper has a financial or personal relationship with other people or organisations that could inappropriately influence or bias the content of the paper.

Acknowledgements

We wish to thank Dr. Hanne Gredal and Dr. Thomas Eriksen for their constructive comments on the manuscript.

Appendix: Supplementary material

Supplementary data to this article can be found online at doi:10.1016/j.tvjl.2016.12.008.

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