UNIVERSIDADE DE LISBOA

Faculdade de Medicina Veterinária

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DISSERTAÇÃO DE MESTRADO INTEGRADO EM MEDICINA VETERINÁRIA

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Resumo

A estenose lombossagrada degenerativa é a compressão da *cauda equina* causada pela protusão de tecidos de suporte no canal vertebral. Apesar de também poder afetar gatos, cães de raça grande, machos e jovens adultos parecem ter predisposição para esta doença. Quando o tratamento médico não promove o alívio dos sinais clínicos associados à estenose lombossagrada degenerativa, o tratamento cirúrgico é uma escolha frequente. Apesar de já terem sido descritas diversas técnicas cirúrgicas para o tratamento de estenose lombossagrada degenerativa, não há critérios definitivos para a escolha de uma ou outra técnica.

A análise crítica é o exame sistemático da evidência científica para verificar a sua fiabilidade, o seu valor e relevância em determinado contexto. É, portanto, essencial para a tomada de decisões fundadas em prática clínica. Os principais objetivos deste estudo foram os de apreciar criticamente a literatura que relata os resultados do tratamento cirúrgico de estenose lombossagrada degenerativa, de identificar lacunas no conhecimento e justificar a necessidade de mais investigação acerca do tema e ainda propôr elementos que poderão valorizar a execução e o relato de informação destes estudos. Foi construída uma ferramenta de análise crítica que examina a execução e o relato de informação de cada estudo e, após uma pesquisa sistemática e seleção da literatura, 17 artigos foram analisados criticamente. Os resultados mostraram que 94% dos estudos incluídos não relataram claramente critérios de inclusão e exclusão e em 71% não foi claro se a inclusão dos participantes foi feita de forma consecutiva. 94% dos estudos relatou a idade, a raça e o sexo dos participantes e 65% não relatou a duração e prevalência dos sinais clínicos. Em 76% dos estudos, a doença não foi medida de forma padronizada e repetível. O diagnóstico da doença foi auxiliado por radiografia em 88% dos estudos, tomografia computorizada em 29%, e ressonância magnética em 53%. Foi considerado que 47% dos estudos incluídos não descreveram claramente a intervenção cirúrgica. Em 35% dos estudos foram usadas medidas objetivas para avaliação dos resultados e todos os estudos incluídos forneceram orientação clínica prática ao leitor.

Apesar de se situarem numa posição relativamente baixa na hierarquia da evidência e possuírem diversas limitações, os resultados demonstram que há lugar para melhorar a execução e o relato de informação em séries de caso, de forma a que se possam gerar e analisar dados rigorosos, para informar a investigação científica, guiar a prática clínica e, acima de tudo, melhorar a prestação de cuidados de saúde em medicina veterinária.

Palavras-chave: cão, estenose lombossagrada degenerativa, síndrome de *cauda equina*, doença lombossagrada, análise crítica, tratamento cirúrgico.

Abstract

Degenerative lumbosacral stenosis (DLSS) is the compression of the *cauda equina* caused by protrusion of supportive tissues into the vertebral canal. Young adult, male, and large-breed dogs seem to be predisposed to this condition, although it can also affect cats. When medical treatment fails to provide adequate relief of clinical signs associated with DLSS, surgical treatment is often performed. Although several surgical modalities to treat DLSS have been reported, definitive criteria for surgical technique preference are currently lacking.

Critical appraisal is the process of systematically examining research evidence to judge its trustworthiness, its value and relevance in a particular context. Therefore it is essential to make informed decisions in clinical practice. The main objective of this study was to critically appraise the literature reporting the results of surgical treatment of DLSS; to identify gaps in current knowledge and ensure there is justification for future research on the subject; and to propose study characteristics that would enrich the conduct and reporting of these studies. A critical appraisal tool that examined the conduct and reporting of each study was designed. After a systematic search and screening of the literature, 17 papers were critically appraised. Results showed that 94% of included studies did not clearly report inclusion and exclusion criteria and in 71% it was unclear whether consecutive inclusion of participants was applied. 94% of studies reported age, breed, and sex of the participants, and 65% did not report duration and prevalence of clinical signs. In 76% of studies, the condition was not measured in a standard and reliable way. Identification of the condition was performed using radiography in 88% of studies, CT in 29%, and MRI in 53%. It was considered that 47% of included studies did not clearly describe the intervention. Objective outcome measures were used in 35% of studies and clinical practical guidance was provided by all included studies.

Although case series rank relatively low in the evidence hierarchy and have several limitations, results demonstrate that there is room for improvement of the conduct and reporting quality of case series so that rigorous data can be generated and analysed, to inform research design, guide clinical practice, and improve veterinary healthcare delivery.

Keywords: dog, degenerative lumbosacral stenosis, *cauda equina* syndrome, lumbosacral disease, critical appraisal, surgical treatment.

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List of abbreviations and symbols

% - Percent

C_{1-7} – cervical vertebrae 1 through 7.

T_{1-13} – thoracic vertebrae 1 through 13.

L_{1-7} – lumbar vertebrae 1 through 7.

S_{1-3} – Sacral vertebrae 1 through 3.

$Ca_{1-20(23)}$ - Caudal vertebrae 1 through 20(23).

CARE – Case report

CT – Computed tomography

Cm - Centimetre

DLSS – Degenerative lumbosacral stenosis

IL-6 - Interleukin 6

IL-β - Interleukin beta

MRI – Magnetic resonance imaging

TNF-α - Tumor necrosis factor alpha

Training report

I underwent my curricular training for the Integrated Masters in Veterinary Medicine between the period of 28th September 2015 and 18th December 2015 at Chestergates Veterinary Specialists, a small animal referral practice in Chester, UK, under the supervision of Dr. François Saulnier-Troff and co-supervision of Prof. Luís Miguel Carreira, summing up to a total of approximately 600 hours. During that period, I rotated through the internal medicine, diagnostic imaging, neurology, and surgery departments, as well as the intensive care unit of the practice.

The emphasis of my training resided in the surgery department. There, I had the opportunity to participate in the preoperative preparation of the patient, surgical procedures, and postoperative patient care. Among the various orthopaedic procedures I collaborated in are: tibial tuberosity advancement, closing wedge ostectomy, lateral suture, tibial plateau leveling osteotomy, stifle and elbow arthroscopy, total hip replacement, tibial crest transposition, and diverse fracture repairs; neeurosurgery procedures included: mini-hemilaminectomy, hemilaminectomy, ventral slot, and lateral foraminotomy by partial iliac osteotomy; and also aided in the following soft tissue surgery procedures: gastropexy, tumor excisions, porto-systemic shunt ligation, unilateral arytenoid lateralisation, soft palate and nare resection, perineal urethrostomy, ovariohysterectomy, mastectomy, cholecystectomy, laparotomy, cystopexy, total ear canal ablation, and anal sacculectomy; amongst others. Patient induction, intubation, and anesthetic monitoring were also part of my routine activities, under the supervision of an experienced anesthetist. In the diagnostic imaging department, I was able to assist and interpret exams mainly from conventional and contrast-enhanced radiography, ultrasound, and magnetic resonance imaging, as well as some computed tomography images, under the supervision of experienced veterinary diagnostic imagers. I participated in patient consultations in the neurology and internal medicine departments, in diagnostic imaging procedures such as endoscopy and colonoscopy, and collection of cerebrospinal fluid.

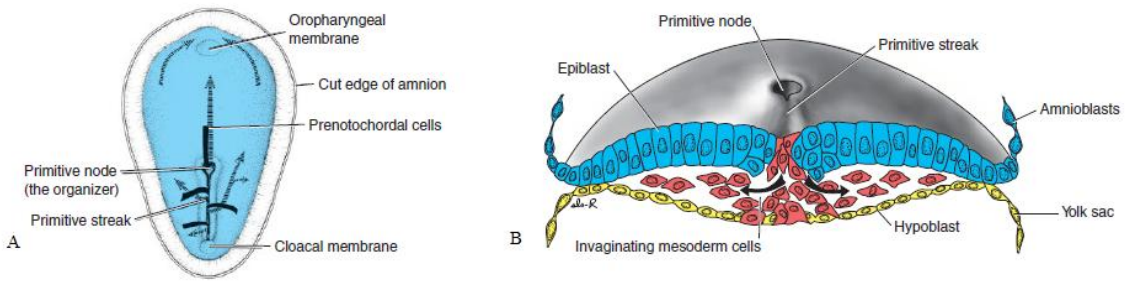
I also had the opportunity to attend two lectures held by Chestergates Veterinary Specialists, as part of their continuous professional development program. One was a thoracic and abdominal interactive x-ray film reading session, given by Virginie De Busscher (DVM, DipECVDI, MRCVS); the other by François Saulnier-Troff (DVM, DipECVS, MRCVS), entitled “Pathophysiology of lumbosacral stenosis, and advances in surgical management”, which inspired me to write this dissertation.

I. Introduction

1. Embryology of the vertebral column

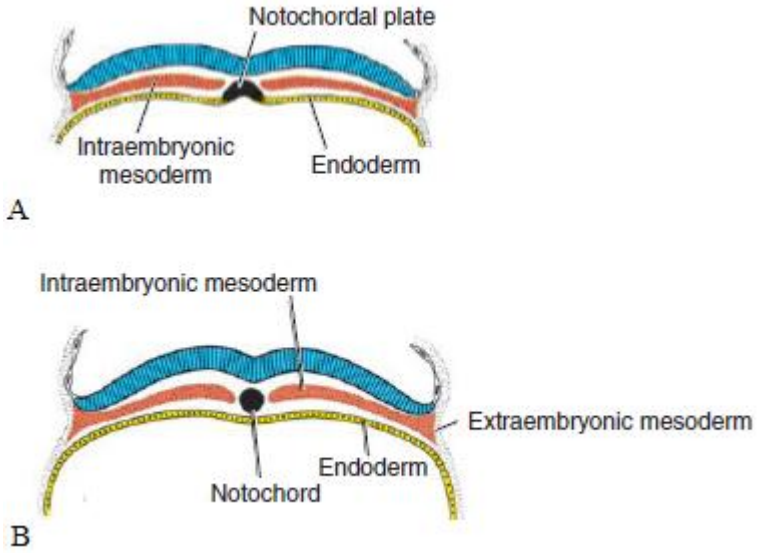
Development of the body's form begins during gastrulation (Kaplan, Spivak & Bendo, 2005). Gastrulation, or germ layer formation, is a stage of embryological development during which the single layered blastula is converted into a trilaminar structure consisting of an outer ectodermal, a middle mesodermal, and an inner endodermal layer (McGeady, Quinn, Fitzpatrick, Ryan & Cahalan, 2006a). Cells in these three layers will originate all of the tissues and organs in the embryo. The primitive streak, well defined germ layers and the notochord also develop during gastrulation. The notochord and somites are the most significant structures responsible for the development of the future vertebral column. Epiblastic cells migrate from the deep surface of the primitive streak and form the embryonic endoderm. Furthermore, cells continue to migrate from the primitive streak, originating the embryonic mesoderm. The embryonic ectoderm consists of the cells that remain on the epiblastic side of the embryonic disc. The migration of these cells from the primitive streak is thought to be induced by multiple embryonic growth factors. A group of specialised cells that migrate through the primitive node, which is located at the cranial end of the primitive streak, gives rise to the prechordal plate and notochordal process (figure 1). Cells of the notochordal process align themselves to create a notochordal plate, which will subsequently fold to form the notochord (figure 2). The notochord will be an early representation of the future vertebrae and bony skeleton. On both sides of the notochord, the mesoderm differentiates into three main areas: paraxial, intermediate and lateral mesoderm (Kaplan et al., 2005; Sadler, 2012d).

Figure 1 - A. Dorsal view of the germ disc. Illustration of the migration of surface epiblast cells from the primitive node and streak (black lines) and between the hypoblast and epiblast (broken lines). **B.** Transverse view of the germ disc, showing inward migration of epiblast cells to create the endoderm. The remaining epiblast cells form the mesoderm (adapted from Sadler, 2012).



Cells with a mesenchymal morphology of different origins give rise to all skeletal tissues. The sclerotomal portion of the mesodermal somites originates the segmented axial skeleton in the trunk. The appendicular skeleton arises from mesenchyme of the lateral plate mesoderm (Carlson, 2009b).

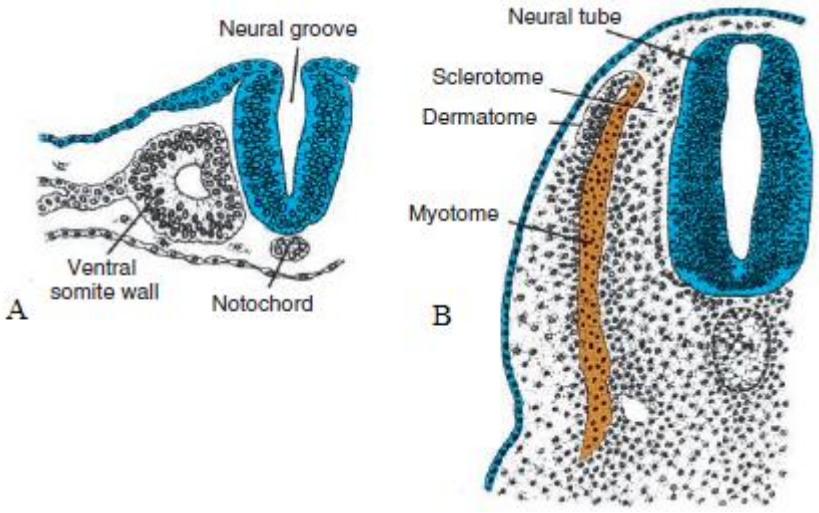
Figure 2 - Transverse sections of the germ disc showing formation of the notochord **A.** The notochordal plate folds and detaches from the endoderm to form the definitive notochord. **B.** The definitive notochord (in black), endoderm (in yellow), mesoderm (in red), and ectoderm (in blue) of the embryonic disc (adapted from Sadler, 2012).



Somites are bilateral segmental transient structures, which derive from paraxial mesoderm and are located laterally to the developing neural tube and notochord. These structures are formed in a cranio-caudal sequence, and are essential for the segmental arrangement of the spinal column and the associated spinal nerves. The outlines of somites first become visible during the third week of gestation in domestic animals (McGeady et al., 2006b). The important components of somite formation are periodicity, epithelialisation, specification, and differentiation. The first somites appear in the anterior portion of the trunk, and new somites "bud off" from the rostral end of the paraxial mesoderm at regular intervals. Although all the somites look identical, they will form different structures at different positions along the anterior-posterior axis (Gilbert, 2000). The number of somite pairs, which is constant for a given species, is usually one pair per vertebra. In domestic animals, differentiation of somites starts around the fourth week of gestation. When somite formation is complete, by the fifth week of gestation, somites formed at an earlier stage have already undergone further differentiation (McGeady et al., 2006b). When the somite is first separated from the

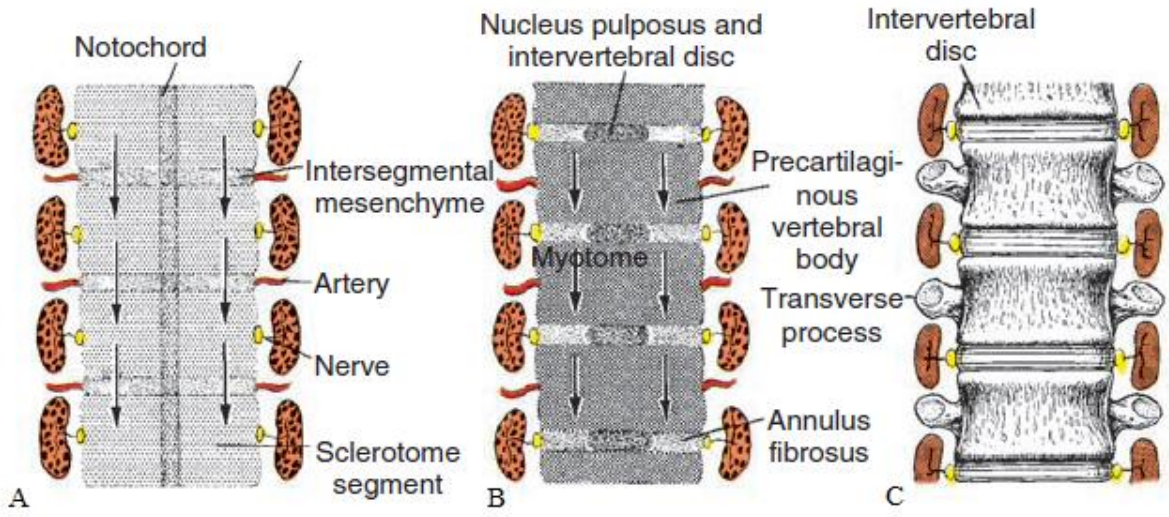
presomitic mesoderm, its cells can become any of the somite-derived structures. However, as maturation occurs, its various regions become committed to forming only certain cell types (Gilbert, 2000). Initially, cells located in the centre of a somite are arranged in an undefined pattern and those at the periphery have the appearance of epithelial cells. The epithelial-like cells of the medial and ventral walls of each somite lose their epithelial appearance and differentiate into mesenchymal cells. Each somite develops into two parts: a sclerotome and a dermomyotome (Kaplan et al., 2005; McGeady et al., 2006b). Cells of the ventral and medial walls of somites undergo differentiation and give rise to connective tissue, such as cartilage and bone, and are called sclerotomes. The epithelial-like cells of the dorsal and lateral walls of each somite give rise to the dermomyotomes. The myotomes originate from the dorso-medial and dorso-lateral borders of the dermomyotomes, and will contribute to the development of the skeletal muscles of the trunk, neck and limbs; the central region of the dermomyotome gives rise to the dermatome, which will form the dermis of the skin (figure 3). The bodies of vertebrae develop from mesenchymal cells derived from the sclerotomal division of somites, but the actual manner of formation is not fully understood. Differentiation of the somites is influenced by factors produced by adjacent structures, including the notochord, neural tube, lateral plate mesoderm and surface ectoderm. Sclerotomal cells lose their intercellular adhesion molecules and undergo transformation into mesenchymal cells (McGeady et al., 2006b). These cells migrate around the spinal cord and notochord to unite with cells from the opposing somite on the other side of the neural tube (Sadler, 2012b).

Figure 3 - Somite differentiation. **A.** Somites are located laterally to the developing neural tube and notochord. **B.** Myotomes, dermatomes and sclerotomes develop from the differentiating somite (adapted from Sadler, 2012).



Sadler (2012b) suggested that as development continues, the caudal half of each sclerotome grows into and fuses with the cephalic half of each subjacent sclerotome in a process called resegmentation. Each vertebra is formed from the combination of the caudal half of one somite and the cranial half of its adjacent somite. Mesenchymal cells between cephalic and caudal parts of the original sclerotome segment fill the space between two precartilaginous vertebral bodies, thus contributing to the arrangement of the intervertebral disc. Resegmentation results in the bridging of the intervertebral discs by the myotomes, allowing them to move the spine. For the same reason, intersegmental arteries, which originally lie between the sclerotomes, now pass midway over the vertebral bodies. Spinal nerves come to lie near the intervertebral discs and leave the vertebral column through the intervertebral foramina (figure 4) (Sadler, 2012b).

Figure 4 - Vertebrae formation. **A.** Resegmentation, in which adjacent sclerotome segments fuse (arrows). **B.** Arrangement of the intervertebral disc and relocation of intersegmental arteries and nerves. **C.** Complete formation of successive vertebrae, interposed with intervertebral discs (adapted from Sadler, 2012).



Currently, it is proposed that no resegmentation occurs and that vertebral bodies arise from chondrogenic centres originating in unsegmented sclerotomally-derived mesoderm which surrounds the notochord throughout its entire length. Cells, which migrate medially and ventrally from the sclerotomes on either side of the neural tube, form a continuous tube of mesenchymal cells, the perichordal tube, which completely surrounds the notochord. Initially, these cells are uniformly distributed but later they undergo differential proliferation and organise, within the sclerotomes, in alternating series of dense caudal accumulations of cells and less dense rostral accumulations (McGeady et al., 2006b). The intervertebral disc will form between these two layers of cells. The cells of the dense accumulations migrate to form

the annuli fibrosi of the intervertebral discs. The developing intervertebral discs divide each sclerotome level and force the remaining cells from a given densely packed layer to fuse with the loosely packed cells of the adjacent caudal level. Thus, one complete vertebra requires two somites to interact properly with each other in order to develop normally (Kaplan et al., 2005). The bodies of the vertebrae and the intervertebral ligaments develop from the less dense cellular accumulations of the perichordal tube. Cells from the dense regions of the sclerotomes on either side of the perichordal tube, which migrate and surround the neural tube, meet dorsally forming each primordial vertebral arch. Each arch, in turn, fuses with its corresponding vertebral body. The primordia of the vertebral processes and, in the thoracic region, ribs, also originate from cells in the dense regions of the sclerotomes. The lower cell density of rostral regions facilitates neural crest cell migration and also permeation by spinal nerves and intersegmental blood vessels (McGeady et al., 2006b). Each vertebra has a complex and unique morphology specified by controls operating at several levels and during several developmental periods.

Mesenchyme of the primordial vertebrae is replaced by cartilaginous templates which, in turn, suffer endochondral ossification at specific periods during embryogenesis (McGeady et al., 2006b). By day 25 of gestation the vertebral column consists of individual chondrified elements similar to definitive vertebrae (Evans & De Lahunta, 2013b). Each vertebra (except the atlas and the axis) is ossified from three primary centres, one for each neural arch or half of the vertebral arch and one for the vertebral body or centrum (Evans & De Lahunta, 2013b; McGeady et al., 2006b). In early stages, formation of centra and neural arches differs. However, later growth and ossification implies perichondral and endochondral ossification. Endochondral ossification of the Beagle vertebral column is possible to observe at 38 days in the thoracic and lumbar regions. Ossification of intervening centra occurs rapidly in both directions from C_2 through L_6. By day 40, lumbar and the first sacral centra are present and by day 43 all three sacral centra are present. Lateral to S_1 and S_2 there are ancestral forms of sacral “ribs” which suffer supplementary ossifications. Growth and fusion, subsequently, result in a combined sacrum dominated by S_1, with its large auricular surface for articulation with the ilium. Perichondral neural arch ossifications occur in pairs. They first appear at 38 days in the cervical region and increase in a craniocaudal sequence. Right and left ossification centres rarely differ in their time of formation. By day 42 the sequence of neural arch ossifications becomes discontinuous because some caudal neural arches show premature ossification before sacral neural arches (Evans & De Lahunta, 2013b). Secondary centres of ossification develop cranial and caudally within the body of each vertebra. Prior to complete

osseous fusion between the body and arch of each vertebra, which occurs after birth, proliferation of the cartilage between the centres of ossification facilitates growth of the vertebrae. Each vertebral process has a separate centre of ossification. Remnants of the notochord become incorporated into the body of each vertebra (McGeady et al., 2006b). The portions of the notochord which persist in each intervertebral region expand, contributing to the nuclei pulposi of the intervertebral discs (Sadler, 2012b; McGeady et al., 2006b). Mesenchymal cells arranged around each nucleus pulposus form an annulus fibrosus (McGeady et al., 2006b).

Muscle embryology may be studied by determination and differentiation of individual muscle cells, through muscle tissue histogenesis or by the morphogenesis of entire muscles (Carlson, 2009b). Myotomes form in close association with the development of their corresponding vertebrae. By overlapping the intervertebral joint, vertebral musculature contributes to the stabilisation of the vertebral column. Myoblasts are progenitor muscle cells that originate from the myotomes. The myoblasts derived from the dorso-medial region of the myotomes form a structure referred to as the epimere, while a group of myoblasts from the dorso-lateral region of the myotomes form the hypomere. The epimere is located dorsal to the transverse process of the developing vertebra, while the hypomere is located ventral to the process. Spinal nerves develop in association with each developing somite, and each nerve gives off a dorsal branch to an epimere and a ventral branch to a hypomere. Each muscle is innervated by more than one spinal nerve because most skeletal muscles of the body derive from more than one myotome. Because they derive from somites, epimeres and hypomeres give rise to muscle groups initially arranged along the cranio-caudal axis. Subsequently, the segmentally arranged epimeric muscles fuse, forming the extensor muscles of the vertebral column, which are referred to as the epaxial muscles of the body. The hypomeric muscle bundles proliferate and extend ventrally into the somatopleure of the body wall, forming its primordial musculature, which initially remains segmented. Subsequently, with the exception of those in the thoracic region, the hypomeres fuse. Myoblasts from the hypomeres in the lumbosacral region give rise to the sub-lumbar muscles, the psoas major and minor muscles and the quadratus lumborum muscles. In the sacro-caudal region, myoblasts give rise to the muscles of the pelvic diaphragm, the coccygeus and the levator ani muscles. Muscles which derive from hypomeres are referred to as hypaxial muscles (McGeady et al., 2006b). Several studies have reported differences in cellular properties between the cellular precursors of limb muscles and axial muscles (Carlson, 2009b).

2. Anatomy of the vertebral column

The vertebral column consists of approximately 50 vertebrae. Vertebrae are irregular bones arranged in five different groups: cervical, thoracic, lumbar, sacral and caudal. The first letter of the word designating each group by means of abbreviation, followed by a digit designating the number of vertebrae in the specific group, constitutes the vertebral formula (Evans & De Lahunta, 2013c). The canine vertebral formula is $C_7T_{13}L_7S_3Ca_{20-23}$ (Sisson, 2002). Although it varies within the species, the number of caudal vertebrae for the Beagle is frequently constant at 20. All vertebrae except the sacral vertebrae remain separate and articulate with adjacent vertebrae, thus forming movable joints. The vertebrae aid in the support of the head, provide attachment for the muscles governing body movements and protect the spinal cord and roots of the spinal nerves. The vertebral column as a whole possesses considerable flexibility (Badoux, 2005). With the exception of the sacral region, where there is some delay, longitudinal growth of the vertebral column continues until approximately 12 months of age, when the epiphyses fuse with the bodies of the vertebrae (Dyce, Sack & Wensing, 2010a).

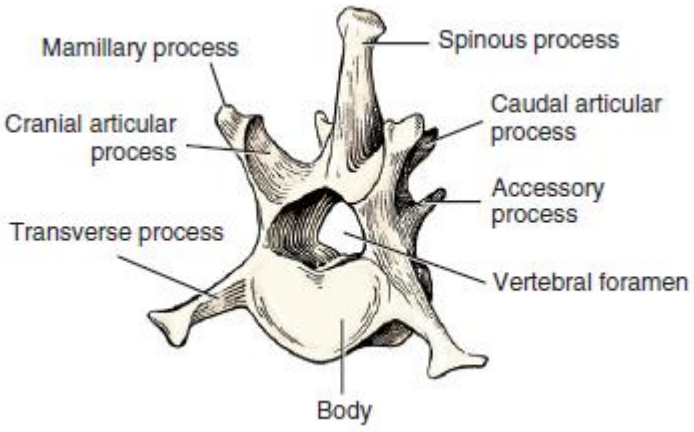
A typical vertebra consists of a body and an arch that completes the enclosure of a vertebral foramen (Dyce et al., 2010a). The vertebral arch consists of right and left pedicles and laminae. Each vertebra also possesses various processes for muscular or articular connections, which may be transverse, spinous, articular, accessory and mammillary (Evans & De Lahunta, 2013c). The body of a typical vertebra is mostly cylindrical, fairly flattened on its dorsal surface, which faces into the vertebral canal and it may present, ventrally, a median crest. It has a slightly convex cranial articular surface and a centrally depressed caudal articular surface (Dyce et al., 2010a). The intervertebral disc consists of fibrocartilage located between adjacent vertebrae. In its centre there are laminae of organised fibrous tissue that constitute the annulus fibrosus, which surrounds the nucleus pulposus, a gelatinous material. The vertebral arch consists of two pedicles and two laminae. The vertebral foramen is the tube that results from the union of the vertebral arch with the vertebral body. The many vertebral foramina coalesce to form the vertebral canal. On each side of the vertebra, the pedicle extends dorsally, from the dorsolateral surface of the body, presenting the cranial and caudal vertebral notches. When the vertebral column articulates, the notches of each side of adjacent vertebrae form the intervertebral foramina, through which pass spinal nerves, arteries and veins (Evans & De Lahunta, 2013c). From lateral to medial, these structures course through exit, middle and entrance zones of each intervertebral foramen (Lanz & Rossmeisl, 2012). Sometimes, an additional lateral vertebral foramen is present in the pedicle near the intervertebral foramen (Dyce et al., 2010a). The dorsal portion of the vertebral arch is

composed of right and left laminae, which unite in the middorsal line to form a spinous process. Each typical vertebra has, on either side, an irregularly shaped transverse process, which projects laterally (Evans & De Lahunta, 2013c). These processes divide the muscles of the trunk into dorsal and ventral divisions (Dyce et al., 2010a). At the cranial and caudal surfaces of the vertebra, at the junction of the pedicle and the lamina, there are paired articular processes. The cranial articular process faces craniodorsally or medially and the caudal process faces caudoventrally or laterally. The interarcuate space is the interval between adjacent arches. The yellow ligament is located dorsally in this space (Evans & De Lahunta, 2013c).

The lumbar vertebrae have longer and more uniformly shaped bodies than the thoracic vertebrae (Dyce, Sack & Wensing, 2010b). Their bodies are dorsoventrally flattened and their width increases from L_1 to L_7, and length from L_1 to L_6 (Sisson, 2002). The body of the seventh lumbar vertebra is approximately the same length as the first. The pedicles and laminae of the lumbar vertebrae resemble those of typical vertebrae of the other regions, however, they are longer and more massive. The spinous processes are highest and most massive in the midlumbar region (Evans & De Lahunta, 2013c). Their height decreases caudally, starting at L_4 (Sisson, 2002). They are approximately half as long, and the dorsal borders are about twice as wide as those of the vertebrae of the cranial thoracic region (Evans & De Lahunta, 2013c). With the exception of the last lumbar vertebra, the lumbar spinous processes are discretely inclined cranially. The transverse processes of the lumbar vertebrae are directed cranially and slightly ventrally, their length increases until L_5 and L_6 and they do not articulate with the sacrum or the adjacent transverse processes. With the exception of L_7, the extremities of the lumbar transverse processes are elongated (Sisson, 2002). The accessory processes are well developed on the first three or four lumbar vertebrae, and absent on the fifth or sixth. They overlie the caudal vertebral notches and extend caudally lateral to the articular processes of the succeeding vertebrae. The articular processes lie predominantly in sagittal planes (Evans & De Lahunta, 2013c). The cranial articular processes are big, compressed laterally and bear mammillary processes (Sisson, 2002). The caudal processes restrict lateral flexion and lie between the cranial processes of succeeding vertebrae (Evans & De Lahunta, 2013c). Other regional features of the lumbar vertebrae are prominent mammillary, and sometimes also accessory, processes (figure 5) (Dyce et al., 2010a).

The sacrum results from the early fusion of the three sacral vertebrae (Sisson, 2002). It is short, wide and wedge-shaped, lies between the ilia and articulates with them. The body of the first sacral segment is larger than the bodies of the other two segments combined.

Figure 5 - Cranial view of the first lumbar vertebra (adapted from Evans & De Lahunta, 2013).

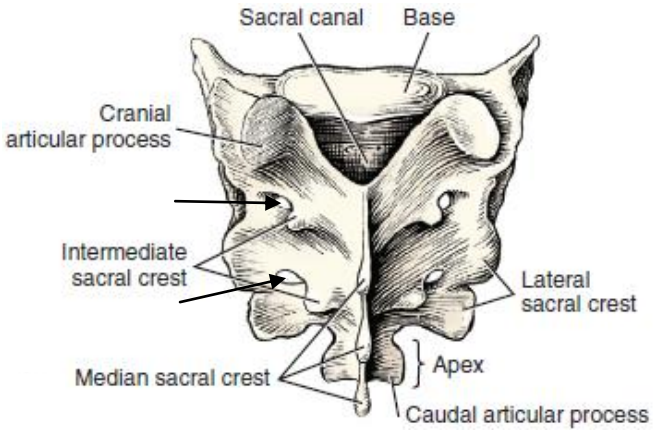


The arched mass with a concave ventral surface that results from the fusion of the three sacral vertebrae is an important obstetric feature (Evans & De Lahunta, 2013c). The median sacral crest develops from the fusion of the three spinous processes of the sacral vertebrae (Sisson, 2002). The crest has two indentations which indicate the areas of fusion. There are two pairs of dorsal sacral foramina in the dorsal surface, through which the dorsal divisions of the sacral spinal nerves and spinal vessels pass. Medial to these foramina are low projections which represent the remnants of the fused mamilloarticular processes of adjacent segments. The collection of the processes and the connective ridges between them forms the intermediate sacral crest. The sacral caudal articular processes are small and articulate with the first caudal vertebra. The cranial articular processes are large, face dorsomedially, and form joints with L_7. The pelvic surface bears two pairs of foramina larger than the corresponding dorsal foramina, situated lateral to the fused sacral bodies. They transmit not only blood vessels, but also the ventral branches of the first two sacral nerves. Lateral to the pelvic sacral foramina there are fused transverse processes. They are greatly enlarged and modified in the first and part of the second segments of the sacrum, in order to articulate with the ilium. The thin lateral sacral crest is formed by the transverse processes of the third and part of the second segments of the sacrum. It terminates caudally in the caudolateral angle, which is flattened and pointed (Evans & De Lahunta, 2013c). The transverse processes of the third sacral segment project caudally and they can fuse or articulate with the first caudal vertebra (Sisson, 2002). The wing of the sacrum is the enlarged, prismatic-shaped lateral portion, which has a rough auricular surface that articulates with the ilium. The base of the sacrum faces cranially, articulating with the last lumbar vertebra, and above its articular surface is the beginning of the sacral canal, which is formed by the coalescence of the three vertebral foramina (Evans & De Lahunta, 2013c). The sacral canal is compressed dorsoventrally (Sisson, 2002). The cranioventral part of the base of the sacrum has a transverse ridge, the promontory. During

birth, the fetuses pass through the pelvic inlet. The dorsal boundary of the smallest part of this bony ring is formed by the promontory and the ilia. The caudal extremity of the sacrum is known as the apex and articulates with the first caudal vertebra. Occasionally, the first caudal vertebra is fused to the sacrum (figure 6) (Evans & De Lahunta, 2013c).

Two adjacent vertebrae with the interposed cartilaginous disc, the articulations between them and the connecting ligaments form a functional unit. This functional unit is complemented by the nerves and blood vessels, leaving the vertebral canal through the intervertebral foramina, and the muscles, covering the cervical, thoracic, lumbar and sacral regions (Liebich & König, 2004a).

Figure 6 - Dorsal view of the sacrum. Note the presence of the dorsal sacral foramina lateral to the intermediate sacral crest (arrows) (adapted from Evans & De Lahunta, 2013).

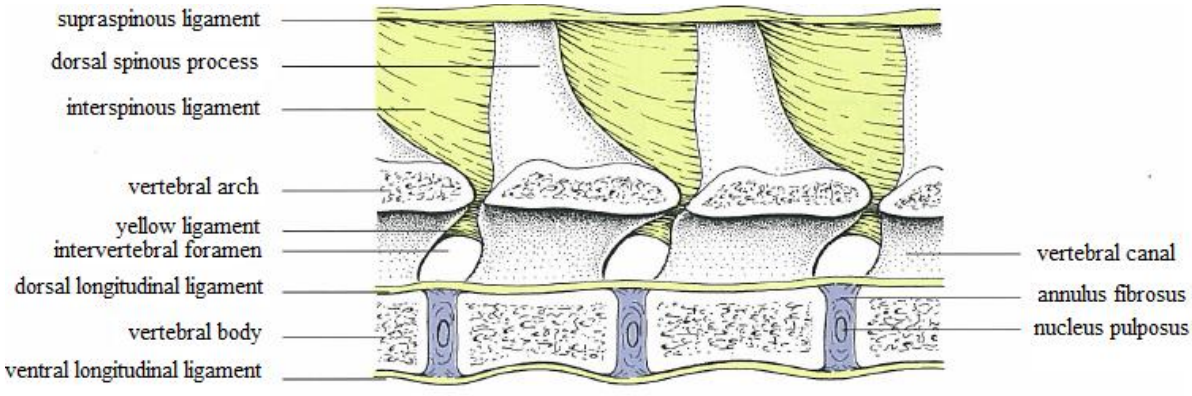


There are two types of joints between vertebrae: one cartilaginous (involving the direct connection of the vertebral bodies) and a synovial one (between articular processes carried on vertebral arches). The space at the lumbosacral junction is about 1 cm in diameter, in a medium-sized dog, and is located, in a transverse plane, about 2 cm deeper than the highest palpable points on the wings of the ilia (Dyce et al., 2010a). With the exception of the intervertebral space between C_1 and C_2, there are thick pads called intervertebral discs located in every intervertebral space, uniting the bodies of adjacent vertebrae. The thickness of the discs is greatest in the cervical and lumbar regions (Evans & De Lahunta, 2013a). The intervertebral discs represent about 16% of the length of the vertebral column of the dog (Dyce et al., 2010a). Each intervertebral disc has an outer fibrous ring, the annulus fibrosus, and a gelatinous, amorphous centre, the nucleus pulposus. The annulus fibrosus is made of bands of parallel fibers that run obliquely from one vertebral body to the next. Stresses and strains required by lateral and dorsoventral movements of the vertebral column are transmitted by this fibrous ring. Near the nucleus pulposus, the annulus fibrosus becomes

more cartilaginous and less fibrous. The annulus fibrosus is one and a half to three times thicker ventrally than dorsally. The nucleus pulposus is a semifluid remnant of the notochord which lies on each end of the vertebral body, surrounded by a line displaced dorsally off-center. Bulging occurs because it is under pressure due to vertebral body movement, when the annulus fibrosus ruptures or degenerates (Evans & De Lahunta, 2013a). There are regional and species variations of the mobility of the synovial joints between the vertebral articular processes. In the caudal thoracic and lumbar regions movement is more or less restricted to flexion and extension due to the radial alignment of the surfaces. The interarcuate ligaments fill the dorsal spaces between the arches of successive vertebrae and may be considered accessory to these joints (Dyce et al., 2010a).

The ligaments of the vertebral column can be grouped into short ligaments, connecting successive vertebrae and long ligaments, spanning several vertebrae, thus forming functional units (Liebich & König, 2004a). Three long ligaments extend along considerable portions of the vertebral column: the supraspinous, the ventral longitudinal and the dorsal longitudinal ligaments (Dyce et al., 2010a). The supraspinous ligament is a thick band, especially in the thoracic region. It attaches to the apices of the spines as it passes through them (Evans & De Lahunta, 2013a), merges with the tendons of the epaxial muscles (Dyce et al., 2010b) and extends caudally from the spinous process of the first thoracic vertebra to the third caudal vertebra. During flexion of the vertebral column, the supraspinous ligament prevents abnormal separation of the spines, along with the thin interspinous ligaments, which send some strands to its ventral surface (Evans & De Lahunta, 2013a). The ventral longitudinal ligament is located ventral to the surfaces of the vertebral bodies from the axis to the sacrum and attaches to each of the intervertebral discs (Liebich & König, 2004a). The dorsal longitudinal ligament is thicker than the ventral longitudinal ligament and lies on the dorsal surfaces of the bodies of the vertebrae, forming part of the floor of the vertebral canal (Evans & De Lahunta, 2013a). It is narrow over the middle of each vertebral body, widens where it crosses each intervertebral disc and extends from the dens of the axis to the sacrum (Dyce et al., 2010b). The intertransverse ligaments are only distinct in the lumbar region, unite the transverse processes of the lumbar vertebrae, and are tensed during lateral flexion and rotation (Liebich & König, 2004a). The yellow ligaments lie between the arches of adjacent vertebrae. They blend with the articular capsules surrounding the articular processes. Ventral to this ligament is the epidural space, which separates the ligaments and arches of the vertebrae from the dura covering the spinal cord (figure 7) (Evans & De Lahunta, 2013a).

Figure 7 - Long and short ligaments of the vertebral column (adapted from Liebich & König, 2004).



The epaxial muscles, or dorsal musculature, associated with the vertebral column and ribs, provide extension and allow lateral movement of the trunk when acting only on one side of the vertebral column. The organisation of these epaxial muscles is complex and there are considerable variations in the literature. The erector spinae muscles are the dorsal muscles that include the epaxial muscles located on the dorsal surface of the vertebral column and ribs. They encompass three longitudinal systems: iliocostalis, longissimus and spinalis. The *iliocostalis muscles* are located laterally to the other epaxial muscles, forming a narrow longitudinal mass that runs cranioventrally over many segments (Hermanson, 2013). These muscles are relatively thin and have only lumbar and thoracic parts (Liebich, Maierl & König, 2004b; Dyce et al., 2010b). The caudal fascicle of these muscles constitutes the lumbar portion, represented by the *iliocostalis lumborum muscle*, which arises from the ilium and contributes to the fixation of the vertebral column and lateral movement when only one side contracts. The longissimus muscle is the major portion of the epaxial muscle mass and lies medial to the *iliocostalis muscle*, extending from the ilium to the head. It has lumbar, thoracic, cervical, atlantal and capital regional divisions (Hermanson, 2013). Its lumbar portion arises from the wings of the ilium and the lumbar spinous processes (Dyce et al., 2010b) and corresponds to the *longissimus lumborum muscle*, which allows extension and stabilisation of the vertebral column (Liebich et al., 2004b). The *transversospinalis muscle* is a muscle mass composed of many different fascicles that join one or more vertebrae, primarily located medial to the iliocostalis and longissimus muscles and lateral to the spinalis, interspinalis, and intertransversarius groups. It is composed by the *semispinalis*, the *multifidus* and the *rotatores muscles*. The lumbar part of the *multifidus muscle* contributes to the fixation of the vertebral column, especially in bilateral action. It consists of a series of muscle bundles that arise from the mammillary process of the first caudal vertebra, the rudimentary articular processes of the sacrum, and the mammillary processes of the lumbar vertebrae and last two thoracic vertebrae

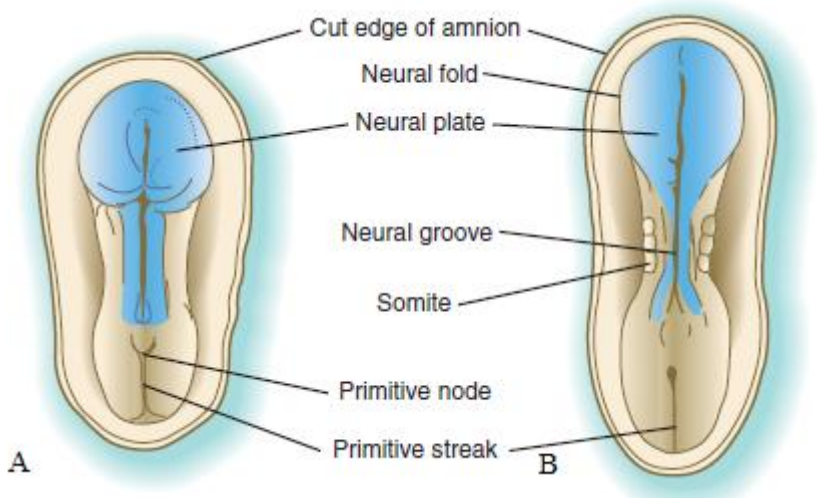
(Hermanson, 2013). Each bundle passes over two segments, thus the insertions are to the spinous processes of the sixth lumbar to the tenth thoracic vertebrae (Dyce et al., 2010b). The *interspinalis muscles* support ventroflexion of the vertebral column (Liebich et al., 2004b) and are separable into lumbar, thoracic and cervical portions. The lumbar division is covered by the *multifidus muscle*. The *intertransversarii muscles* are segments split off from the longissimus system. They have caudal, lumbar, thoracic and cervical parts and pass over one, two or three vertebrae, between transverse processes, between articular and transverse processes or between mammillary and transverse processes. These muscles overlap in the lumbar (*intertransversarii lumborum muscles)* and thoracic (*intertransversarii thoracis muscles*) regions (Hermanson, 2013). The lumbar hypaxial muscles lie on the ventral surfaces of the lumbar vertebrae and ilium, insert on the os coxae and femur, and include the *psoas minor, psoas major,* and *quadratus lumborum*. The *psoas minor muscle* runs ventromedially towards the pelvis, lies between the iliac fascia and the peritoneum ventrally and the *psoas major* and *quadratus lumborum* muscles dorsally. It arises from the bodies of the last thoracic and first four to five lumbar vertebrae (Dyce et al., 2010b). The *psoas major muscle* is located dorsal to the *psoas minor* and ventral to the *quadratus lumborum*. It arises from the transverse processes of L_2 and L_3, lying medial to the *quadratus lumborum muscle.* It attaches ventrally to L_3 and L_4, and to the ventral and lateral surfaces of L_4 to L_7. As it passes the cranioventral border of the ilium, the caudal portion of the *psoas major muscle* receives the *iliacus muscle* from the ventral surface of the ilium. These two muscles compose the *iliopsoas muscle*. When the femur is fixed in position, these three muscles allow flexion and fixation of the vertebral column (Hermanson, 2013). The *quadratus lumborum muscle* is the most dorsal of the lumbar hypaxial muscles and lies directly ventral to the bodies of the last three thoracic vertebrae and the bodies and transverse processes of all the lumbar vertebrae and inserts on the medial surface of the wing of the ilium (Dyce et al., 2010b). It is covered ventrally by the *psoas minor* caudal to L_1 and caudal to L_4 by the *psoas major*. The *quadratus lumborum* is active in flexion and fixation of the lumbar vertebral column (Hermanson, 2013).

3. Embryology of the spinal cord

Throughout much of its development, the spinal cord preserves its fundamental organisation, making it a useful tool to study the structural and functional features of the central nervous system (Carlson, 2009c). After gastrulation, the ectodermal germ layer has the shape of a disc, broader in the cephalic than in the caudal region (Sadler, 2012d). In domestic animals, at the end of the third week of embryological development, the notochord induces thickening of the overlying columnar ectodermal cells to become pseudostratified neuroepithelial cells, thus

forming the neural plate (McGeady et al., 2006c). Cells of the plate arrange to make up the neuroectoderm, and this phenomenon induces neurulation. The process through which the neural plate originates the neural tube is called neurulation (Sadler, 2012c). Progessive changes in the columnar neuroepithelium originate folding of the neural plate (McGeady et al., 2006c). Notochord-induced changes at the median angle seem to largely influence plate bending. Many explanations have been proposed for lateral folding of the neural plate and it is now apparent that it is the result of numerous region-specific mechanisms intrinsic and extrinsic to the neural plate (Carlson, 2009a). In this phenomenon, the edges of the neural plate elevate to form the neural folds, originating the neural groove at the depressed midregion that forms during that process (Sadler, 2012c). Cellular proliferation at the medial aspects of the neural folds causes their median approach and results in fusion, which begins in the cervical region, at the level of the fourth somite, and then progresses cranially and caudally (figure 8) (McGeady et al., 2006c).

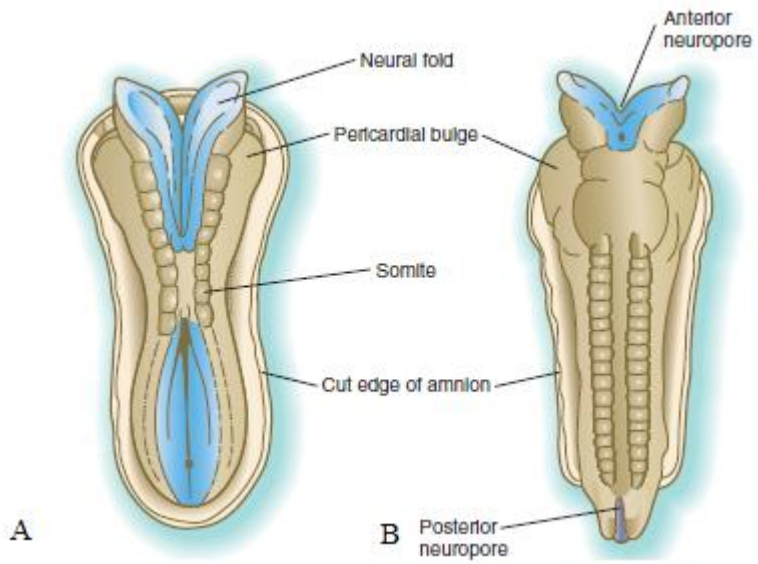
Figure 8 - Dorsal view of the developing embryo. **A.** At the beginning of the third week of development, the central nervous system is a plate of thickened ectoderm. **B.** By the end of the third week of development, neurulation commences (adapted from Carlson, 2009).



As the neural folds suffer elevation, cells at the lateral border or crest of the neuroectoderm, begin to dissociate from their neighbors. This cell population, the neural crest, suffers an epithelial-to-mesenchymal transition and leaves the neuroectoderm by migration and displacement (Carlson, 2009c; Sadler, 2012c). Migration of neural crest cells is influenced by intrinsic properties of these cells and also features of the external environment encountered during this movement (Carlson, 2009c). After migration from the neural tube, neural crest cells form cellular aggregations in a dorsal position, extending along the length of the neural tube on either side. A single pluripotent neural crest cell can differentiate into many cell types

depending on its location within the early embryo (McGeady et al., 2006c). Until complete fusion is accomplished, the cephalic and caudal ends of the neural tube communicate with the amniotic cavity by an anterior or cranial and posterior or caudal neuropores, respectively (Sadler, 2012c). At this stage, the developing central nervous system has limited vascular supply, so it has been suggested that these structures receive their supply of nutrients from the amniotic fluid through the neuropores (figure 9). Closure of the anterior neuropore occurs at approximately midway through the embryonic period and the posterior neuropore closes shortly afterwards, thus completing neurulation (McGeady et al., 2006c). Prior to this phenomenon, the future spinal cord and brain are already recognisable (Carlson, 2009c). Neural tube formation in the sacral and caudal regions occurs through secondary neurulation.

Figure 9 - Dorsal view of the embryo undergoing neurulation. **A.** The neural folds suffer elevation and start fusing in the cervical region. **B.** Formation of the extremities of the neural tube, the anterior and posterior neuropores (adapted from Carlson, 2009).



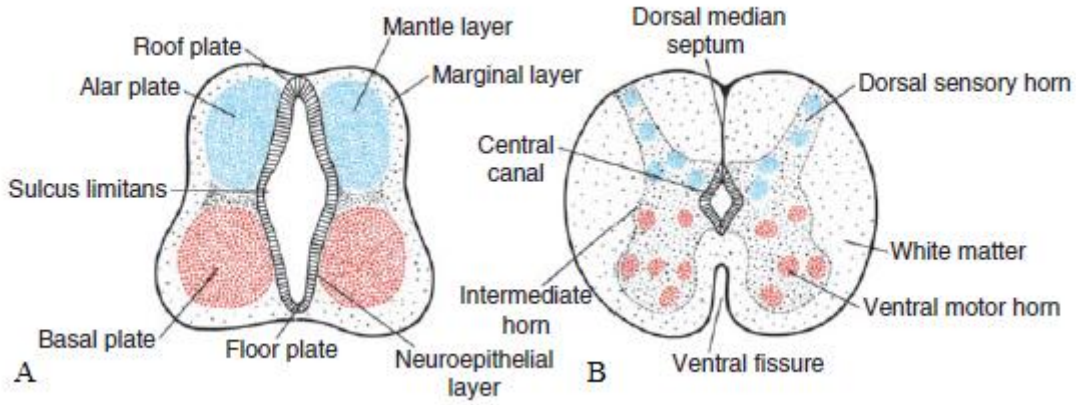
A column of mesenchymal cells, derived from the primitive streak in the caudal region of the embryo, fuses with the closed caudal end of the neural tube, forming a cavitary central canal in this cord of cells. This structure becomes continuous with the neural canal that resulted from the primary neurulation (Dellman & McClure, 1986; McGeady et al., 2006c; Carlson, 2009a). Besides giving rise to subcutaneous, mammary and pituitary glands and enamel of the teeth, the ectodermal germ layer is also responsible for the development of the central and peripheral nervous systems, the sensory epithelium of the ear, nose and eye; and the epidermis, including hair and nails (Sadler, 2012d). By the end of neurulation, the central nervous system is represented by a tubular structure with a narrow caudal portion, the spinal cord, and a much broader cephalic portion with a number of dilations, the brain vesicles

(Sadler, 2012c). These vesicles are continuous with the lumen of the spinal cord, the central canal.

Neural tube neuroepithelial cells give rise to two cell types: neuronal and glial progenitor cells (McGeady et al., 2006c). Gliablasts originate supporting cells, while neuroblasts suffer differentiation and further development into adult nerve cells, the neurons of the central nervous system (McGeady et al., 2006c; Sadler, 2012a). Upon differentiation of its cells, the neural tube is composed of three layers: an inner ependymal or ventricular layer, a middle mantle or intermediate layer and an outer marginal layer. Neuroblasts, through outward migration from the ependymal layer, give rise to the mantle layer. This area is later responsible for the formation of the gray matter of the spinal cord (McGeady et al., 2006c; Carlson, 2009c). Nerve fibers emerging from neuroblasts in the mantle layer give rise to the marginal layer. After myelination of its nerve fibers, this layer acquires a white appearance, making it the white matter of the spinal cord. Proliferation of neuroblasts in the mantle layer causes ventral and dorsal thickening of each side of the neural tube (McGeady et al., 2006c; Carlson, 2009c; Sadler, 2012a). The dorsal thickenings, referred to as alar plates, form sensory areas. Axons of the alar plates penetrate into the marginal layer of the cord and ascend to higher or lower levels to form association neurons. The ventral thickenings or basal plates form the motor areas of the spinal cord and contain ventral motor horn cells. Axons of neurons in these plates break through the marginal zone and become visible on the ventral aspect of the cord. They conduct impulses from the spinal cord to the muscles and are known as the ventral motor root of the spinal nerves. The boundary between the two is a longitudinal groove called the *Sulcus limitans* (Sadler, 2012a). Cell division causes expansion of the alar and basal plates, which results in fusion of these four plates, forming the butterfly-shaped gray area characteristic of the cross-section of the spinal cord (McGeady et al., 2006c). The dorsal and ventral midline areas of the neural tube, known as the roof and floor plates, respectively, serve as pathways for nerve fibers crossing from one side of the spinal cord to the other and do not have neuroblasts (Sadler, 2012a). The notochord exerts a very important effect on the organisation of the dorsal and ventral roots that enter and leave the spinal cord, due to its action on the floor plate. If it is absent, recognisable dorsal and ventral roots will also be absent (Carlson, 2009c). A group of neurons accumulates between the dorsal and ventral horns, becoming the intermediate horn. This horn contains neurons of the sympathetic portion of the autonomic nervous system and is present only at thoracic (T_1- T_{12}) and upper lumbar levels (L_2 or L_3) of the spinal cord (figure 10).

After production of neuroblasts ceases, neuroepithelial cells form the gliablasts, which migrate from the neuroepithelial layer to the mantle and marginal layers. In the mantle layer, they differentiate into protoplasmic astrocytes and fibrillar astrocytes, located between blood vessels and neurons, providing support and having metabolic functions (Sadler, 2012a). Oligodendroglial cells, originally found in the marginal layer, form myelin sheaths around the ascending and descending marginal layer axons, and are also thought to originate from gliablasts (McGeady et al., 2006c; Carlson, 2009c; Sadler, 2012a). Microglial cells are highly phagocytic cells derived from vascular mesenchyme when blood vessels grow into the nervous system. They appear in the second half of development. After ceasing to produce neuroblasts and gliablasts, neuroepithelial cells differentiate into ependymal cells lining the central canal of the spinal cord and the brain ventricles (McGeady et al., 2006c).

Figure 10 - Development of the spinal cord. **A.** Neural tube layers after differentiation: marginal layer, mantle layer and ependymal layer (neuroepithelial layer). **B.** Formation of the white and gray areas of the spinal cord. The alar plates form sensory areas and the basal plates form motor areas (adapted from Sadler, 2012).



Sensory ganglia or dorsal root ganglia of the spinal nerves, the sensory components of the peripheral nervous system, arise from lateral migration of neural crest cells (McGeady et al., 2006c; Sadler, 2012a). Neuroblasts of the sensory ganglia form centrally and peripherally growing processes. The first penetrate the dorsal portion of the neural tube to, in the spinal cord, either end in the dorsal horn or ascend through the marginal layer to one of the higher brain centres. These processes are called dorsal sensory root of the spinal nerve. The peripherally growing processes participate in formation of the trunk of the spinal nerve by joining fibers of the ventral motor roots. These processes terminate in the sensory receptor organs. Dorsal root neurons therefore originate from neuroblasts of the sensory ganglia derived from neural crest cells. Neural crest cells also differentiate into sympathetic

neuroblasts, Schwann cells, pigment cells, odontoblasts, meninges and mesenchyme of the pharyngeal arches. Peripheral nerves are myelinated by Schwann cells originated from the neural crest (McGeady et al., 2006c; Sadler, 2012a). Motor nerve fibers arise from the basal plate nerve cells, collecting in bundles to form ventral nerve roots (Sadler, 2012a). During this developmental period, few neurons differentiate in the caudal end of the cord, which results in the tapering of the spinal cord and gives rise to the conus medullaris. Caudal to this structure, the spinal cord is composed of a strand of glial and ependymal cells, which attaches the conus medullaris to the caudal vertebrae. As a result of the difference in growth rates of the spinal cord (derived from the ectoderm) and the vertebral canal (derived from the mesoderm) during the foetal period, the newborn animal has a longer spinal column than the spinal cord. Therefore, the roots of the spinal nerves arising from the lumbar, sacral and caudal regions of the cord, referred to as *cauda equina*, must pass caudally within the vertebral canal before emerging through the intervertebral foramina (Dellman & McClure, 1986; McGeady et al., 2006c; Budras et al., 2007; Carlson, 2009c; Dyce, Sack & Wensing, 2010c; Meij & Bergknut, 2010).

4. Anatomy of the spinal cord

The central nervous system is composed of the spinal cord and the brain. The vertebral canal encloses the dorsal and ventral spinal roots that belong to the peripheral nervous system and the spinal cord. The spinal cord is elongated, approximately cylindrical (Fletcher, 2013) and extends cranially into the medulla oblongata at the level of the foramen magnum (Dellman & McClure, 1986). It exhibits some degree of dorsoventral flattening and presents anatomical variations throughout its length (Fletcher, 2013). Two thickenings, or intumescences, that give rise to the nerve supply of the limbs, and the final caudal tapering, or conus medullaris, are present in the spinal cord (Dyce et al., 2010b). The neck, trunk and tail, the limbs, and the caudal and dorsal surfaces of the head are innervated by the spinal cord. It has three purposes: to act as a reflex centre, producing subconscious responses of muscles and glands to stimuli; to process afferent information from muscles, tendons, joints, ligaments, blood vessels, skin and viscera, and it discharges efferent commands that control muscles and regulate glands; to conduct information to and from the brain, through a system of axonal tracts, by which the brain receives status information about the neck, trunk and limbs while sending out information that controls posture, movement, and the visceral aspects of behavior (Fletcher, 2013). Throughout the entire length of the spinal cord, the ventral spinal artery runs along the ventral median fissure, providing important arterial supply (Budras et al., 2007). The spinal

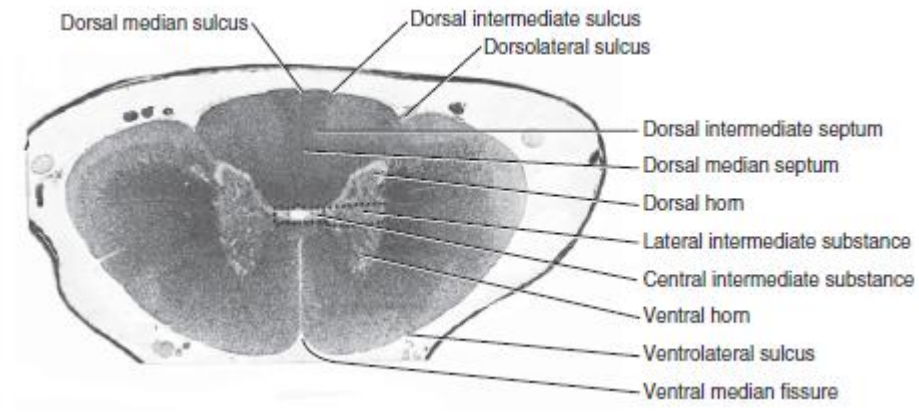
cord may be divided into two parts: gray matter, located deeply in transverse section; and superficially, white matter (Dellman & McClure, 1986).

Three protective layers, the meninges, surround the spinal cord and spinal roots within the vertebral canal. The outer layer, the *dura mater* is a thick and fibrous envelope which, along with the other meningeal layers, through lateral extensions, ensheathes spinal roots (Fletcher, 2013). The dura mater is separated from the periosteum of the skull bones at the level of the foramen magnum to form a tube separated from the margin of the vertebral canal by the epidural space. This space is occupied by fat and the internal vertebral venous plexus, which cushion the spinal cord passively deformed by the curvatures of the vertebral column (Budras et al., 2007; Dyce et al., 2010b). The venous sinuses, one on each side of the floor of the vertebral canal, collect blood from vertebrae, meninges, and nerve roots (Sjöström, 2003). The arachnoid membrane is the thin intermediate meninx, which attaches to the inner surface of the dura mater. It is joined to the pia mater by arachnoid trabeculae that cross the subarachnoid space, which is filled by cerebrospinal fluid. The pia mater is the deepest meninx. It has bilateral thickenings along the spinal cord forming denticulate ligaments. The arachnoid membrane and the pia mater are designated leptomeninges because they are delicate relative to the dura mater. The central canal is filled with cerebrospinal fluid and lined with ependymal cells. Cerebrospinal fluid is usually a clear, colorless, and slightly alkaline liquid derived from blood, mostly of the choroid plexus vessels, and therefore must be returned to the circulating blood. Arachnoid villi and lymphatics associated with nerves are the two major drainage routes for that purpose (Fletcher, 2013).

Gray matter, relatively rich in capillary supply and composed of cell bodies and processes of neurons and glial cells surrounds the central canal (Fletcher, 2013). In transverse sections it resembles the shape of a butterfly or an H (Dellman & McClure, 1986; Budras et al., 2007; Dyce et al., 2010c), having bilateral wings connected across the midline by central intermediate substance. The lateral intermediate substance is the lateral extension of intermediate substance into each gray matter wing. It projects into the surrounding white matter as a lateral horn in the thoracolumbar segments of the spinal cord (Dellman & McClure, 1986; Dyce et al., 2010c; Fletcher, 2013). The dorsal horn is the dorsal extension of the lateral intermediate substance of the gray matter and the ventral horn is the corresponding ventral extension. Sensory or afferent neurons are situated in the dorsal root and have their origin in the dorsal horn. Motor or efferent neurons are located in the ventral root and arise from the ventral horn (Budras et al., 2007). The neurons contained in each horn are grouped according to their functional and topical associations. However, this is not fully perceptible

(Dyce et al., 2010c). The white matter surrounds the gray matter externally in the spinal cord. It includes myelinated, as well as nonmyelinated axons, oligodendrocytes, astrocytes, and blood vessels. The white matter of each half of the spinal cord is divided into three funiculi: dorsal, ventral and lateral (Dyce et al., 2010c; Fletcher, 2013). There is a dorsolateral sulcus where dorsal roots enter the spinal cord and a corresponding ventrolateral sulcus where ventral roots leave the spinal cord. The latter, however, is frequently imperceptible (Dellman & McClure, 1986; Fletcher, 2013). The dorsal funiculus is located between the dorsolateral sulcus, where dorsal rootlets enter the spinal cord, and the dorsal median sulcus. The ventral funiculus is found medial to the ventral root attachments. The lateral funiculus is located between the dorsal and ventral root attachments (Budras et al., 2007; Dyce et al., 2010c; Fletcher, 2013). Ascending and descending nerve fibres, frequently accumulated in bundles of common origin, destination and function, compose the three funiculi (Dyce et al., 2010b). The white commisure connects right and left ventral funiculi. Septae, sulci, and fissures are also featured in the spinal cord (Fletcher, 2013). The spinal cord is divided bilateral and symmetrically by a ventral median fissure and a dorsal median sulcus. The dorsal median septum extends ventrally from the dorsal median sulcus to the central intermediate substance where the central canal is located (Figure 11).

Figure 11 - Transverse section of the spinal cord at the level of C_2. The dorsal funiculus is located between the dorsolateral sulcus and the dorsal median sulcus. The ventral funiculus is located between the ventrolateral sulcus and the ventral median fissure. The lateral funiculus is located between the dorsal and ventral root attachments (adapted from Evans & De Lahunta, 2013).



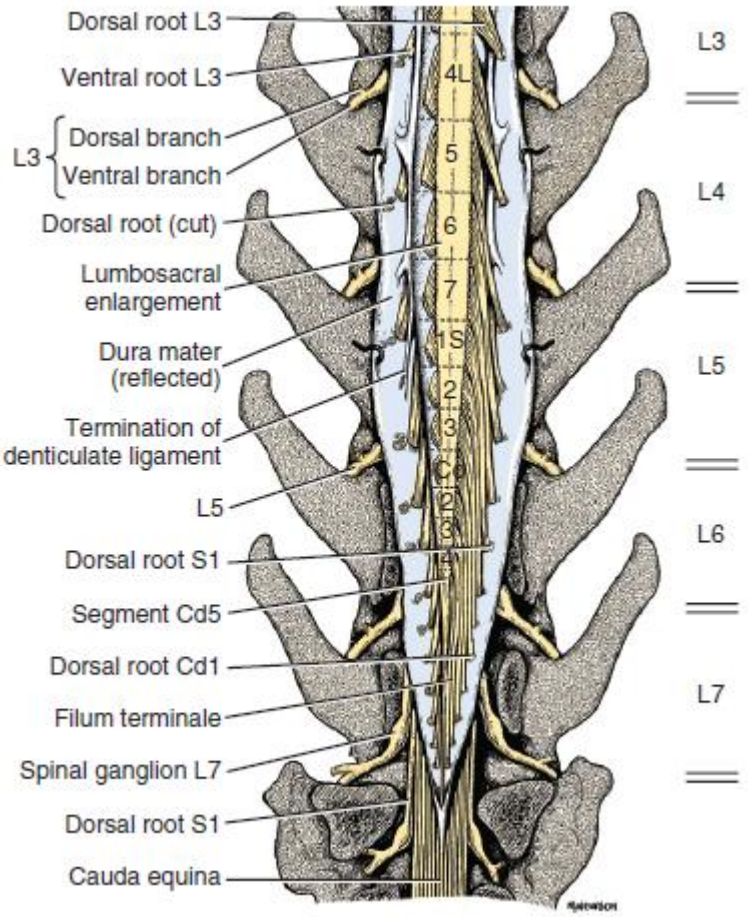
The spinal cord may be divided into segments. A segment corresponds to an area of the spinal cord where a pair of spinal roots from a particular spinal nerve exits or enters the spinal cord (Dellman & McClure, 1986). Spinal cord segments, spinal roots, and spinal nerves are identified numerically, similarly to vertebrae, according to their region. The lumbar intumescence innervates the pelvic cavity and pelvic limbs and involves segments L_5, L_6 and

L_7, and part of segment S_1. Caudal to the lumbar intumescence, at the level of the L_5 vertebra, the spinal cord becomes conical, in what is called the conus medullaris. This region consists of segments S_2, S_3 and from Ca_1 to Ca_5. These segments appear successively smaller, and they are surrounded by caudally directed spinal roots. The conus medullaris is continued by the filum terminale, and beyond it sacral and caudal spinal roots within the vertebral canal stream caudally, exiting at the intervertebral foramina. These roots, along with the filum terminale, are called *cauda equina*, which, in the dog, lie mostly caudal to the lumbar cistern. In the caudal lumbar, sacral, and caudal region, spinal cord segments lie progressively cranial to their respective vertebrae. In medium-sized and large dogs, the conus medullaris ends approximately at the level of L_6 to L_7 intervertebral disc (Budras et al., 2007; Fletcher, 2013).

The L_7, S_1, S_2, S_3 and Ca_1 to Ca_5 nerve segments compose the *cauda equina* (Denny, Gibbs & Holt, 1992; Lanz & Rossmeisl, 2012). As previously noted in the "embryology of the spinal cord" chapter, nerve roots of the *cauda equina* run caudally before leaving their intervertebral foramen. For example, the L_7 nerve root originates from the L_7 spinal cord segment, located at the L_4 or L_5 vertebra. It abandons the dural sac at L_6, and the vertebral canal through the intervertebral foramen of L_7-S_1 (figure 12) (Sjöström, 2003).

The gray matter is composed of neurons, neuroglia (astrocytes and oligodendrocytes, predominantly) and a relatively rich blood supply. Spinal cord neurons may be classified as interneurons, projection neurons, or efferent neurons. Spinal cord interneurons are located between a particular input and the resulting output from the spinal cord, participating in spinal reflexes, locomotion and other voluntary movement. They can be activated by synaptic input from primary afferent neurons, from caudally projecting pathways (originating in the brain), from other interneurons, and from axonal branches of efferent neurons. Interneurons vary in axon size, location and type of action. Spinal cord projection neurons generally form cranial projecting pathways to the brain, by sending axons into the white matter. Activation of these neurons is the result of stimulation of primary afferent neurons of viscera, muscles, joints, or skin (Fletcher, 2013). The excitability of spinal cord projection neurons is influenced by primary afferent neurons, interneurons, and by caudally projecting axons from brain projection neurons. Projection neurons respond mainly to somatic stimulation (skin or muscles and joints), but others respond to both somatic and visceral stimulation (Cervero & Lumb, 1988). Spinal cord efferent neurons send axons through ventral roots to innervate muscles and glands and are categorised as somatic or autonomic (visceral). Cell bodies of preganglionic autonomic neurons are located in the lateral intermediate substance and lateral horn.

Figure 12 - Dorsal view of the relationship between spinal cord segments (numbered in the spinal cord) and vertebrae (L_3 to L_7) after laminectomy and reflection of the dura mater. The nerve roots of the *cauda equina* run caudally before leaving the vertebral canal through the intervertebral foramina (adapted from Evans & De Lahunta, 2013).



Their axons synapse on cell bodies of postganglionic axons located in autonomic ganglia along nerves or in the wall of organs. Neurons in autonomic ganglia innervate cardiac, or smooth muscle or glands. Somatic efferent neurons innervate skeletal muscles. Their cells bodies are located in the ventral horn, grouped into motor nuclei. Alpha motor neurons are somatic neurons that innervate muscle fibers responsible for producing muscle tension. In a clinical context, these motor neurons with an axon that leaves de central nervous system to innervate the target organ are classified as lower motor neurons (Fletcher, 2013). These neurons provide simple reflexes to the limbs but are, in most other circumstances, directed by upper motor neurons. Axons entering the central nervous system by the dorsal roots of the spinal nerves interact with interneurons within the gray matter, and then project on ventral horn cells of the same or neighboring segment to provide local reflex responses (Dyce et al., 2010c). Destruction of neurons responsible for local reflex responses results in flaccid paralysis of the muscles they innervate (Fletcher, 2013). Upper motor neurons are involved in

more complicated reflexes and are also responsible for voluntary movements. They exert their control by excitation or inhibition of lower motor neurons, thus indirectly controlling muscle fibers (Dyce et al., 2010c). There are two other types of somatic efferent neurons, gamma motor neurons, and beta motor neurons. A motor unit is composed of a motor neuron and all of the muscles fibers it innervates. Motor units vary in their properties, according to size. A particular skeletal muscle has all its motor units' neuronal cell bodies grouped together, forming a motor neuron poll within a motor nucleus in the ventral horn (Fletcher, 2013).

Spinal cord neurons with similar functions usually have their cell bodies grouped together, forming longitudinal columns of cells called nuclei, when viewed in transverse sections of the spinal cord. Classification of the spinal cord may be approaches through two perspectives. One involves identification of functionally significant nuclei; the other implies division of the gray matter into ten distinct laminae. Gray matter nuclei may be divided into dorsal horn nuclei, intermediate substance nuclei and ventral horn nuclei (Fletcher, 2013).

The white matter of the spinal cord is composed of myelinated and nonmyelinated axons. Efferent axons that exit the spinal cord through ventral roots, afferent axons that enter the spinal cord through dorsal roots, and axons that compose pathways that carry information cranially and caudally in the spinal cord, form the white matter. Cranially and caudally projecting axons relay information from one location to another typically have a common function and travel together in the white matter. The dorsal and lateral funiculi are separated by the dorsolateral sulcus, which is the entrance zone for dorsal root afferent axons. Afferent axons typically bifurcate in the dorsal funiculus into longer cranial and caudal branches. These branches further bifurcate and penetrate the gray matter to synapse on projection neurons, interneurons, and, in some cases, motor neurons. Afferent axons segregate by size within a dorsal rootlet as they enter the spinal cord. Nonmyelinated and small myelinated axons collect laterally within the dorsal rootlet, conducting impulses from nociceptors, thermoreceptors and certain mechanoreceptors. Larger myelinated axons conduct urgent information from muscles, joints, and skin, and are positioned medially as the rootlet enters the spinal cord. Small afferent axons gather laterally, immediately deep to the dorsolateral sulcus, and their overlapping cranial and caudal branches form a relatively nonmyelinated band called the *tractus dorsolateralis.* Shorter axons lie closer to the gray matter than longer ones. Likewise, spinal tracts that travel to or from the brain are located more peripherally in white matter than are shorter axons that originate in one spinal segment and terminate at another level of the spinal cord. An axonal tract may have axons densely grouped at its centre, but axons become dispersed at the margin, mingling with margins and centres of other tracts.

Some tracts have no distinct centre of high axon density and axons scattered over the white matter. Spinal cord projection neurons have cell bodies in the spinal cord gray mater and axons that travel cranial in a white matter tract. Cranial projecting pathways that terminate in the brain begin with primary afferent neurons that activate spinal cord projection neurons. Cranial projecting tracts relay different types of information to the brain according to the stimulus that activates them. Some spinal cord projection neurons are activated by noxious stimuli, others by specifically nonnoxious mechanical or thermal stimuli. Other projection neurons are activated by both noxious and mechanical stimuli. Some are activated by both visceral and somatic stimulation, while others respond just to the latter (Fletcher, 2013). Cranial projecting tracts can be organised by funiculi. The white matter of the spinal cord can be divided into dorsal funiculus, lateral funiculus and ventral funiculus (Budras et al., 2007; Fletcher, 2013). The dorsal funiculus, unlike the lateral and ventral funiculi, contains mainly axons of primary afferent neurons, relatively few axons from spinal cord projection neurons and a negligible number of caudally projecting tract axons. The ventral funiculus consists of fiber-tracts which connect different portions of the brain and spinal cord and that cannot be accurately distinguished (Budras et al., 2007).

Throughout the length of the spinal cord, the appearance of the transverse section of spinal cord segments varies. The ratio of white matter to gray matter is greatest in the cervical segments and gradually declines caudally, with the exception of the segments that innervate the limbs, due to the absence of caudal and cranial projecting axons from white matter tracts. A dorsal median fissure is consistent in lumbar and sacral segments. The apex of the dorsal gray horn tends to be rectangular in the lumbosacral region and a lateral gray horn is evident in thoracic and cranial lumbar segments of the spinal cord (Fletcher, 2013). The level at which the spinal cord ends varies among species. In the dog it is within L_6 or L_7 (Dyce et al., 2010c).

5. Degenerative lumbosacral stenosis

Degenerative lumbosacral stenosis (DLSS) is the compression of the *cauda equina* caused by protrusion of supportive tissues into the vertebral canal (Dewey, 2013). The clinical signs associated with pathological conditions of the lumbosacral region which include malformation, growth disturbance, degeneration, compression, inflammation, infection, displacement, and reduced circulation are collectively described as *cauda equina* syndrome. Several different terms have been used in the literature to describe conditions of the lumbosacral region. Lumbosacral instability, lumbosacral spondylopathy, spondylolisthesis, and lumbosacral malarticulation-malformation, have been described as DLSS, which is the most common cause of *cauda equina* syndrome seen in clinical practice (Denny et al., 1982;

Watt, 1991; Sjöström, 2003; Lanz & Rossmeisl, 2012). The many different terms that have been used to report the disease may indicate that it is of multifactorial origin. The anatomical structures involved may be the last lumbar vertebra, the sacrum, the lumbosacral disc, the soft tissue structures around the lumbosacral joint, and the *cauda equina* and associated nerve roots (Sjöström, 2003). Compression of the *cauda equina* may be caused by: Hansen type II disc protrusion, congenital osseous stenosis of the vertebral canal or foramina, lumbosacral osteochondrosis, proliferation of the joint capsules or ligaments, osteophytosis or spondylosis, epidural fibrosis, and instability, malalignment or subluxation of L_7-S_1 (Sisson, Le Couteur, Ingram, Park & Child, 1992; Schmid & Lang, 1993; Jones et al., 1999; Hanna, 2001; Sjöström, 2003; Lanz & Rossmeisl, 2012). Less commonly reported causes of lumbosacral disease include synovial and ganglion cysts, tethered cord syndrome and tumours (Denny et al., 1982; Webb, Pharr, Lew & Tryon, 2001; Sharp & Wheeler, 2005b; Forterre et al., 2006; Lanz & Rossmeisl, 2012; De Decker et al., 2015; Schmökel & Rapp, 2016).

DLSS may affect animals of any breed, sex, or age. However, young adult, male, and large-breed dogs seem to be predisposed to this condition. In most dogs, the vertebral column slopes slightly downward toward the tail. German Shepherd dogs show a much larger slope, making them walk with strongly flexed stifles and hocks (Dyce et al., 2010b). Although there has been variation on breed disposition reports, German Shepherd dogs appear to be most frequently affected (Danielsson & Sjöström, 1999; Linn, Bartels, Rochat, Payton & Moore, 2003; Lanz & Rossmeisl, 2012). Heavy work (police, military) and the use of dogs in training (sporting dogs) have also been reported as risk factors (Ness, 1994; Jones et al., 1996b; Jones, Banfield & Ward, 2000a; Linn et al., 2003; Sharp & Wheeler, 2005b; Worth, Thompson & Hartman, 2009). Hansen type II intervertebral disc disease, osseous stenosis, malformations and transitional vertebrae, although rare, have also been sporadically reported in cats at the lumbosacral level (Hurov, 1985; Sharp & Wheeler, 2005b; Harris & Dhupa, 2008; Lanz & Rossmeisl, 2012).

5.1. Pathophysiology

The lumbosacral joint is subject to considerable biomechanical forces due to its role as a "hinge" between the pelvis and the sacrum. Its main movements are flexion and extension. Lateral and rotational movements are limited (Sjöström, 2003; Gradner, Bockstahler, Peham, Henninger & Podbregar, 2007; Dyce et al., 2010b). The lumbosacral segments of the vertebral column have a significantly high range of motion. Therefore, it is proposed that lumbosacral joint chronic instability may play a role in the pathogenesis of degenerative processes that may be associated with DLSS (Jones, Davies, Werre & Shackelford, 2008; Meij & Bergknut,

2010; Dewey, 2013). Biomechanical changes in the vertebral column due to degenerative conditions may also contribute to the progression of the disease (Schmid & Lang, 1993; Gradner et al., 2007; Lanz & Rossmeisl, 2012). Abnormal mobility may also be a result of damage to the intervertebral disc or other supportive structures (Morgan & Bailey, 1990). Given the complexity of motion of the lumbosacral joint, it is not fully understood how degenerative changes at that level influence the pathogenesis of DLSS. A systematic method for detection of lumbosacral instability and its pathological effects is currently unavailable, which complicates the management of this disease. The degree and type of *cauda equina* compression directly influences the specific pathological events that contribute to the development of the disease and associated clinical signs of motor weakness, pain or other sensory alterations (Rydevik, Brown & Lundborg, 1984; Benninger et al., 2004). Physical deformation caused by compression may result in nerve fiber demyelination, axonal loss, and nerve root ischemia. Inflammatory cell infiltration, wallerian degeneration of the nerve roots and intraradicular edema can equally occur (Kobayashi, Yoshizawa & Yamada, 2004a; Jones et al., 2008). Spinal cord compression may also be responsible for the release of proinflammatory cytokines and growth factors, such as tumor necrosis factor alpha (TNF-α), interleukin 6 (IL-6), and interleukin beta (IL-β), thus contributing to the further progress of the disease, induction of neuropathic pain and spinal sensitisation. This occurs through the activation of spinal cord glial cells and astrocytes (Rothman, Huang, Lee, Weisshaar & Winkelstein, 2009). In vivo models simulating long-term *cauda equina* compression have shown that it can result in anterograde, retrograde and transneuronal degeneration of the spinal cord. This phenomenon may originate damage not only at the compression site, but also to dorsal root ganglia and ventral horn motor neurons (Marsala, Sulla, Jalc & Orendacova, 1995; Kobayashi, Yoshizawa & Yamada, 2004b).

Sjöström (2003) proposed a theory for the evolution of DLSS, in which biomechanical factors, age, congenital malformation of the lumbosacral vertebrae or sacroiliac joint, result in disc degeneration, initiating at the level of the nucleus pulposus. This originates disc collapse, with concurrent narrowing of the space between L_7 and S_1. Dorsal synovial joint collapse follows, with subluxation of the articular processes. When the annulus fibrosus, the interarcuate ligament, and the joint capsule of the articular process joints become lax, they lose part of their stabilising functions. Osteophyte formation between the vertebral bodies and around the synovial joints is thought to be a result of instability. Secondarily, there is sclerosis of vertebral body end-plates, degenerative arthritis of synovial joints, and thickening of the interarcuate ligament and of the joint capsules, which can cause narrowing of the vertebral

canal and loss of mobility of the lumbosacral region. Intervertebral disc degeneration results in bulging of the annulus fibrosus dorsally into the vertebral canal, the intervertebral foramina, or both. Ventral subluxation of the sacrum also contributes to the narrowing of the vertebral canal.

DLSS is often a painful condition. Pain may be of discogenic, osteoarthritic, meningeal, or radicular origin (Ness, 1994; Jones et al., 1996b; Danielsson & Sjöström, 1999; Sjöström, 2003). Because the *cauda equina* is relatively resistant to compression, discogenic pain is thought to be the main source of pain in DLSS (Danielsson & Sjöström, 1999). Neurological signs originate from the compression of the *cauda equina* nerve roots or of the L_7 nerve root where it leaves the intervertebral foramen. Compression of the lumbosacral nerve roots can be perpetuated by various pathological changes: bulging of the disc or annulus fibrosus (figure 13-A), thickening of the dorsal annulus fibrosus (figure 13-B), subluxation of L_7-S_1 (figure 13-C), osteophytosis in the spinal canal and around the articular process joints (figure 13-D), thickening of the joint capsule of the articular process joints (figure 13-E), and thickening of the interarcuate ligament (figure 13-F) (Sjöström, 2003).

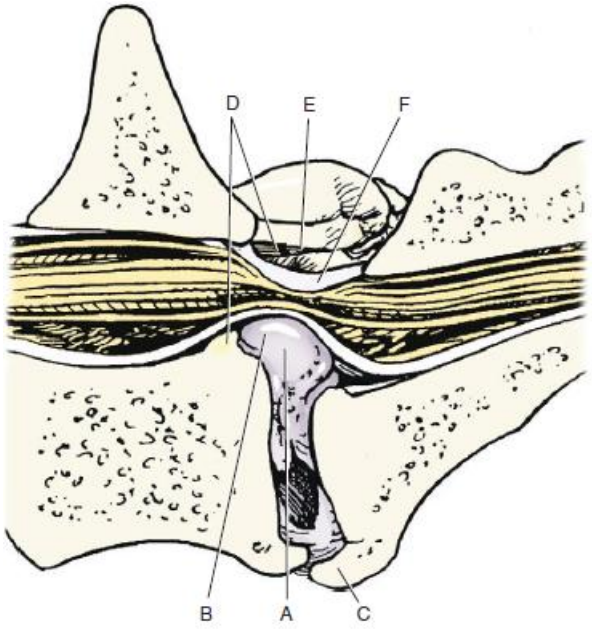
Transitional lumbosacral vertebrae may result in asymmetry between the sacroiliac joints, resulting in rotation of the pelvis. This may originate a narrower vertebral canal with overloading of the intervertebral disc, resulting in early degeneration. It has been demonstrated that there is a correlation between lumbosacral transitional vertebrae and DLSS and German Shepherd dogs appear to be overrepresented in this condition (Morgan, Bahr, Franti & Bailey, 1993; Morgan, 1999).

5.2. Clinical signs and physical examination

Clinical signs of lumbosacral disease are highly nonspecific and can be persistent or episodic and heterogeneous (Danielsson & Sjöström, 1999; Meij & Bergknut, 2010; Lanz & Rossmeissl, 2012). Patient history usually includes lower lumbar or pelvic limb pain, which may manifest in different ways, such as: crouched pelvic limb posture, pelvic limb lameness, pelvic limb root signature (figure 14-A), and self-mutilation of the limbs, genitals, or tail. Back pain is usually the first and most typical sign of lumbosacral disease (Meij & Bergknut, 2010; Lanz & Rossmeissl, 2012).

Low back pain is different from that manifested in thoracolumbar lesions (Sharp & Wheeler, 2005b). It can be triggered by extension of the lumbosacral joint, such as in jumping exercises, climbing stairs, standing from a prone position, and crawling.

Figure 13 - Pathological changes associated with DLSS that may contribute to *cauda equina* compression (adapted from Lanz & Rossmeisl, 2012).

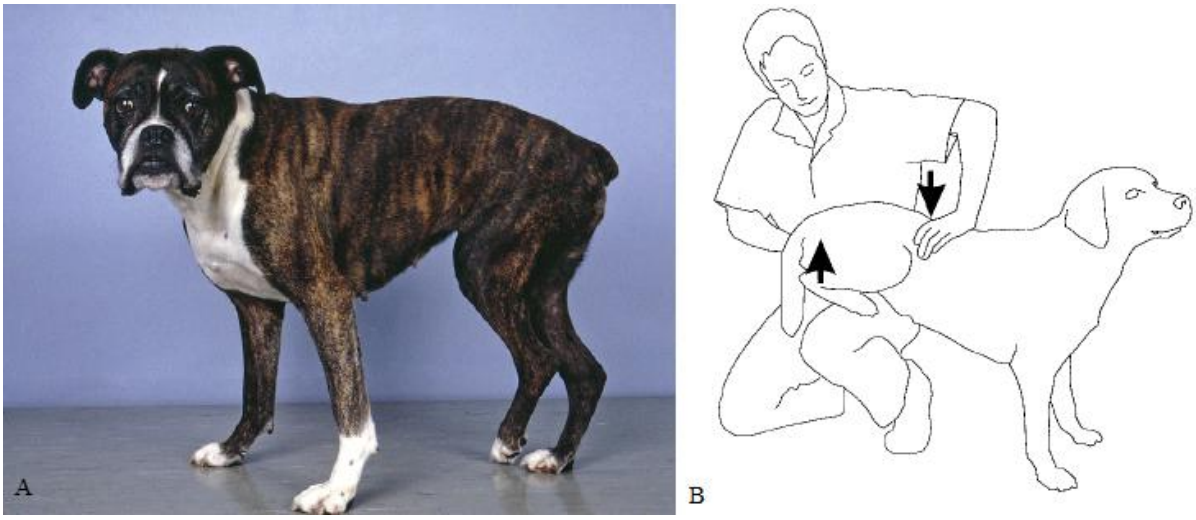


Unwillingness to exercise or jump into a car, stiffness during physically demanding exercise, scuffing of the toenails of the pelvic limbs (Ness, 1994; Danielsson & Sjöström, 1999; Sjöström, 2003; Dewey, 2013), intermittent lameness or limb dysfunction exacerbated by activity, or lower motor neuron neurological deficits may indicate DLSS (Sharp & Wheeler, 2005b). Clinical signs may be bilateral or unilateral. Limb or back hyperesthesia, difficult to differentiate from pain with origin in a concurrent orthopaedic condition, may be present at physical examination (Lanz & Rossmeissl, 2012; Dewey, 2013). A complete orthopaedic examination may rule out concomitant problems, such as hip or stifle arthrosis. The patient may show stiffness of the musculature surrounding the lumbosacral region (Sjöström, 2003). Mental changes may also be noted (Danielsson & Sjöström, 1999). There are several techniques to isolate lumbosacral painful responses: traction or elevation of the tail; per rectum application of pressure to the L_7-S_1 disc space; elevation of the animal's thoracic limbs off the ground, making sure it is in an extended position, followed by percutaneous application of pressure to the lumbosacral space; performing the hyperextension or lordosis test, which consists in elevating the pelvic limbs off the ground, guaranteeing extension of the hips, and applying lumbosacral pressure (Figure 14-B); and rotation of the lumbosacral joint by swinging the rear limbs bilaterally.

Pelvic limb neurological signs, sphincter tone and anal reflex depend on the level and severity of neurological damage (Sjöström, 2003; Sharp & Wheeler, 2005b; Lanz & Rossmeissl, 2012). Neurological dysfunction in the pelvic limbs can range from paraplegia, paraparesis,

monoplegia or monoparesis to mild proprioceptive deficits which do not affect gait (Watt, 1991; Sharp & Wheeler, 2005b; Lanz & Rossmeissl, 2012).

Figure 14 - Clinical signs and physical examination **A.** Boxer with pelvic limb root signature characteristic of DLSS (adapted from Meij & Bergknut, 2010). **B.** Hyperextension or lordosis test. The pelvic limbs are elevated and supported while direct digital pressure is applied to the lumbosacral space (adapted from Sjöström, 2003).



Neurological deficits depend on nerve root involvement and may differ between right and left sides. When present, they are lower motor neuron in nature. A shortened and stiff stride of the pelvic limbs may be observed. Dragging the claws of the pelvic limb digits and ataxia are manifestations of decreased proprioception (Sjöström, 2003). The sciatic, cranial tibial, gastrocnemius, anal, and flexor withdrawal reflexes may be normal, depressed or absent. If significant sciatic deficits are present, failure of hock flexion during withdrawal reflex testing may occur. Muscle atrophy of neurological origin may be observable in the sciatic distribution. Patellar reflex testing may exhibit a false exaggerated response, also called patellar pseudohyperreflexia. This is due to loss of antagonistic muscle tone in dogs with significant sciatic nerve deficits (Ness, 1994; Lanz & Rossmeissl, 2012; Dewey, 2013) and must be differentiated from the increased reflex that occurs with upper motor neuron deficits observed in lesions cranial to the L_4 segment (Sharp & Wheeler, 2005b). The tail may be flaccid or carried low due to pain, hypotonia, or paralysis. Occasionally, urinary and fecal incontinence may be the only clinical manifestations of lumbosacral disease (Watt, 1991; Danielsson & Sjöström, 1999; Sjöström, 2003; Meij & Bergknut, 2010; Dewey, 2013). Urinary incontinence commonly manifests itself as a lower motor neuron sign, with dribbling of urine and an easy manual expression of the bladder. Fecal incontinence is associated with poor anal tone, and may be present even with a normal anal reflex (Sharp & Wheeler, 2005b).

Incontinence is most commonly a result of pelvic and pudendal nerve dysfunction (S_1-S_3), which causes urethral or anal sphincter hypotonia and possibly altered sensation in the perineal region (Sharp & Wheeler, 2005b; Lanz & Rossmeissl, 2012).

5.3. Differential diagnoses

Several clinical conditions may cause similarly unspecific and heterogeneous signs seen in DLSS (Lanz & Rossmeisl, 2012). Differential diagnoses depend if the signs are unspecific or if obvious neurological deficits are present (Sharp & Wheeler, 2005b). The differential diagnoses list may be narrowed down through the neurological examination of the animal, depending on the presence, type, and severity of neurological deficits that arise from the L_4-S_3 or *cauda equina* region (Lanz & Rossmeisl, 2012). It might be challenging to differentiate lesions in the L_4-S_3 nerve roots from L_4-S_3 lesions within the dural sac (Sharp & Wheeler, 2005b). It is not infrequent for an older dog to have more than one disease entity, which may hamper the diagnosis. Orthopaedic conditions such as hip dysplasia with secondary osteoarthritis, bilateral cranial cruciate ligament disease, psoas muscle injury, gracilis or semitendinous muscle contracture; or other neurological diseases, commonly found in breeds affected with DLSS, may mimic or exaggerate signs of lumbosacral disease, and therefore should always be considered (Mckee, 1993; Sjöström, 2003; Meij & Bergknut, 2010). Dogs with orthopaedic disease have a normal neurological examination. In degenerative myelopathy, there are no signs of pain, the withdrawal reflex is normal, but the patellar reflex may be depressed (Sharp & Wheeler, 2005b). However, multifocal myelopathy, mainly in the T_3-L_3 and L_4-S_3 spinal cord segments and *cauda equina*, has been observed in geriatric large-breed dogs with concurrent evidence of lumbosacral disease. In dogs with DLSS showing proprioceptive ataxia and deficits, multilevel type II thoracolumbar intervertebral disc disease, degenerative myelopathy, and neoplasia should also be considered (Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012). DLSS, discospondylitis and neoplasia may not be possible to differentiate on physical examination (Sharp & Wheeler, 2005b). Vertebral osteomyelitis, polymyositis, polyarthritis, and fracture should also be considered (Dewey, 2013).

5.4. Diagnosis

The diagnosis of DLSS should be based on a complete patient history and clinical signs and subsequent performance of careful physical, orthopaedic, and neurologic examinations. A definitive diagnosis should be supported by radiological and advanced imaging results (Sharp & Wheeler, 2005b; Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012).

5.4.1. Imaging techniques

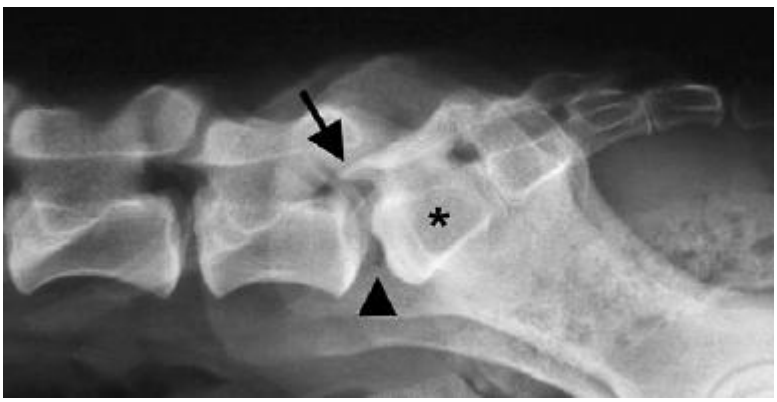
Multiple diagnostic imaging modalities have been used to diagnose DLSS. These include conventional and stress radiography, myelography, epidurography, transosseous and intravenous venography, discography, linear and computed tomography, and magnetic resonance imaging. Computed tomography (CT) and magnetic resonance imaging (MRI) have become valuable tools to diagnose DLSS since they have proven to be sensitive and specific detectors of *cauda equina* compression in dogs. Myelography, epidurography and discography are still commonly used, although they often lack sensitivity. Epidurography and discography are sometimes difficult to interpret (Ramirez & Thrall, 1998; Meij & Bergknut, 2010; Dewey, 2013). Although normal radiographs do not exclude DLSS (Morgan & Bailey, 1990; Ramirez & Thrall, 1998; Scharf, Steffen, Grünenfelder, Morgan & Flückiger, 2004; Steffen, Hunold, Scharf, Roos & Flückiger, 2007), radiography is often the first diagnostic test performed in dogs with clinical signs of lumbosacral disease (Mattoon & Koblik, 1993; Meij & Bergknut, 2010). Dogs without clinical signs of lumbosacral disease may have imaging findings consistent with DLSS. There is also no apparent correlation between the degree of *cauda equina* compression evident on imaging and the severity of disease (Dewey, 2013). CT and MRI are accurate in the diagnosis of DLSS. They may be particularly helpful in the diagnosis of lateralised disc protrusions that fail to be detected by other imaging modalities. However, because they provide highly detailed information, they can also lead to overinterpretation of findings. Moreover, their availability and cost limit their use in veterinary practice (De Risio, Thomas & Sharp, 2000; Sjöström, 2003).

5.4.1.1. Conventional radiography

Radiographic studies should extend from the L_4 vertebral level to the caudal vertebrae to allow examination of the entire lumbosacral region and *cauda equina* nerve roots (Sharp & Wheeler, 2005b; Lanz & Rossmeisl, 2012). Both lateral and ventrodorsal views should be obtained (Sjöström, 2003), although lateral is the most informative view in case of DLSS (McKee, 1993; Meij & Bergknut, 2010). Due to individual and breed variations in normal range of motion, vertebral canal diameter, and size of the L_7-S_1 intervertebral disc space, dynamic radiographs of the lumbosacral space have limited diagnostic value for DLSS (Lanz & Rossmeisl, 2012). Although they can be used to show instability and abnormal movement at the lumbosacral joint, stress radiography studies may be challenging to interpret (Mattoon & Koblik, 1993; McKee, 1993; Schmid & Lang, 1993; Sjöström, 2003). Survey radiographs may be a helpful diagnostic tool to exclude discospondylitis, neoplasia, fracture, luxation, idiopathic lumbosacral stenosis or other causes of pelvic limb dysfunction which may mimic

cauda equina syndrome. Abnormal radiographic findings of the lumbosacral region, such as spondylosis, disc space collapse, lumbosacral instability, and abnormal angulation of the spine, have been detected in large-breed and geriatric dogs without clinical signs of lumbosacral disease. Therefore, although they are commonly found in dogs with DLSS, these findings are not exclusive or indicative of *cauda equina* compression (Morgan & Bailey, 1990; Mattoon & Koblik, 1993; McKee, 1993; Sjöström, 2003; Steffen et al., 2007; Meij & Bergknut, 2010). Sclerosis of the vertebral end plates, osteophytes around the lumbosacral joint, elongation of the sacral lamina into the caudal aperture of L_7, ventral subluxation of S_1, and the vacuum phenomenon are seen in DLSS (figure 15). These, however, cannot be used to make a definitive diagnosis of the disease, since they are also seen in clinically normal dogs (Sjöström, 2003; Meij & Bergknut, 2010). Radiographic evidence of sacral osteochondrosis, transitional vertebrae, and congenital sacral anomalies in a patient with clinical signs of *cauda equina* compression should raise suspicion of compression (Sjöström, 2003; Flückiger, Damur-Djuric, Hässig, Morgan & Steffen, 2006; Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012). Certain important soft tissue changes in DLSS, such as neural tissue compression, are not detected by non-contrast radiography (Morgan & Bailey, 1990; McKee, 1993; De Risio et al., 2000).

Figure 15 - Lateral radiograph of the lumbosacral region in a dog. Note the presence of a transitional vertebra (asterisk), elongation of the sacral lamina into the caudal aperture of L_7 (arrow), and the vacuum phenomenon between L_7 and S_1 (arrowhead) (adapted from Meij & Bergknut, 2010).



5.4.1.2. Myelography

Myelography is a diagnostic imaging modality in which nonionic contrast medium is injected into the subarachnoid space at the cisterna magna or at a caudal lumbar site (L_5-L_6). In myelography, only the dural sac is visualised in the lumbosacral region. Canine patients have a variable and unpredictable site of termination of the dural sac. Therefore, myelography can only successfully be used to assess the *cauda equina* in cases in which the dural sac extends caudally into the sacrum, and this feature is impossible to predict prior to contrast medium

injection (Feeney & Wise, 1981; Lang, 1988; Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012). Inadequate filling of the subarachnoid space due to obstruction or swelling may occur with injection of contrast medium in the cisterna magna. Spine flexion may improve subarachnoid space contrast medium filling (Sharp & Wheeler, 2005b). Injection of contrast medium in the lumbar subarachnoid space may lead to epidural leakage, interfering with the assessment of the lumbosacral vertebral canal. In cases in which the dural sac is elevated from the ventral vertebral floor or the compressive lesion is dorsally located, myelography would not be successful. A laterally compressive lesion involving the intervertebral foramen or the lateral recesses of the intervertebral canal could equally be missed by myelography studies (Ramirez & Thrall, 1998). Thoracolumbar disc disease studies have reported myelography as a more sensitive imaging technique than conventional radiography (Kirberger, Roos & Lubbe 1992; Olby, Dyce & Houlton, 1994). Normal myelography findings do not exclude DLSS (Ramirez & Thrall, 1998; Meij & Bergknut, 2010). False-positive results may also occur (Lang, 1988; Watt, 1991). Myelography can be advantageous when disease localised cranial to the lumbosacral region is suspected. It can also be useful when performed before discography/epidurography to evaluate the spinal cord and *cauda equina* (Lanz & Rossmeisl, 2012). Dynamic studies may increase the sensitivity of myelograms and be valuable in the diagnosis of DLSS (Lang, 1988; Ramirez & Thrall, 1998; Sjöström, 2003). Like survey radiography, myelography may also be useful to exclude pathological changes that may cause clinical signs similar to those of DLSS, such as neoplasia and intervertebral disc disease of adjacent discs (Danielsson & Sjöström, 1999).

5.4.1.3. Discography

When performed together, discography and epidurography are valuable for the detection of lumbosacral lesions. Although not routinely used, discography should precede epidurography (Barthez, Morgan & Lipsitz, 1994). It has also been reported that they are easier to perform than myelography (Ramirez & Thrall, 1998; Lanz & Rossmeisl, 2012). Discography is the injection of contrast medium through the annulus fibrosus into the nucleus pulposus of an intervertebral disc. If the disc has degenerative changes, the contrast medium will leak into it (Wrigley & Reuter, 1984). Abnormal discography findings in the lumbosacral region include: if more than 0.3 milliliters of contrast medium can be injected into the disc; accumulation of contrast medium in the disc; a nonhomogenous contrast uptake within the nucleus pulposus; and focal extravasation of contrast medium into the vertebral canal. The accuracy of discography has been reported as 87% and the technique has been associated with few false-negative results (Sisson et al., 1992; Ramirez & Thrall, 1998; Lanz & Rossmeisl, 2012).

Lateralised or foraminal disc protrusions are more easily detected through discography, when compared to epidurography and myelography (Mckee, 1993; Sjöström, 2003; Lanz & Rossmeisl, 2012). Although there are no reports of neurologic or histologic damage to the intervertebral disc secondary to discography in the dog (Ramirez & Thrall, 1998), some complications have been reported in human patients. These affect a range of 0 to 2,7% of patients undergoing lumbar discography and include transient exacerbation of pain, infectious discitis, and epidural abscess (Walker, Abd, Isaac & Muzin, 2008). In dogs, discography has been associated with the potential to cause spinal cord damage, exarcebate or originate disc degeneration after injection, and extravasation of contrast medium into adjacent soft tissues (Ramirez & Thrall, 1998; Meij & Bergknut, 2010).

5.4.1.4. Epidurography

It is argued that, when not followed by discography, epidurography should be performed between S_3 and Ca_1 because it may avoid potential complications of injection at the lumbosacral junction (Lanz & Rossmeisl, 2012). Injection at the lumbosacral junction may be advantageous if discography will also be performed, however, needle position at the site of interest may interfere with the interpretation of the epidurogram (Ramirez & Thrall, 1998). Dynamic studies may allow a better visualisation of compressive lesions (Sjöström, 2003). A normal epidurogram includes adequate filling of the epidural space and presence of a continuous contrast medium column on the ventral floor of the vertebral canal, on lateral view (Feeney & Wise, 1981). The epidural space may not be adequately filled because it is poorly defined, contains adipose tissue, and due to irregular filling of the lateral recesses (Morgan & Bailey, 1990). This will cause a false-negative result. Neural compression should be suspected if the epidural contrast column is narrowed, deviated, obstructed or elevated to an extent higher than 50% of the diameter of the vertebral canal (Ramirez & Thrall, 1998). Reported sensitivity of epidurography ranges from 42% (Hathcock, Pechman, Dillon, Knecht & Braund, 1988) to 93% (Selcer, Chambers, Schwensen & Mahaffey, 1988) for the diagnosis of lumbosacral disease. A combination of radiography, discography and epidurography has been reported to be an accurate diagnostic method for DLSS in 89% of cases (Barthez et al., 1994).

5.4.1.5. Venography

Venography is the intravenous or transosseous injection of contrast medium into the vertebral venous sinus system (Ramirez & Thrall, 1998; Lanz & Rossmeisl, 2012). Compressive lesions of the spinal cord or vertebral canal are likely to cause compression or displacement of the internal vertebral venous plexus due to its anatomical location (Koblik & Suter, 1981; Ramirez & Thrall, 1998). Position and degree of filling of the internal vertebral venous plexus

may allow for indirect evaluation of possible mass lesions within the vertebral canal. Individual anatomical variations of the configuration of the internal vertebral venous plexus and technical injection errors may challenge interpretation of a venogram (Lanz & Rossmeisl, 2012). Difficulties such as: leakage of contrast medium into the soft tissues or epidural space and failure of the contrast medium to flow into the vertebral sinuses, even in absence of technical errors; have been reported (Blevins, 1980; Hathcock et al., 1988; Ramirez & Thrall, 1998; Dewey, 2013). Therefore, venography is not a routine diagnostic instrument for DLSS (Ramirez & Thrall, 1998; Lanz & Rossmeisl, 2012).

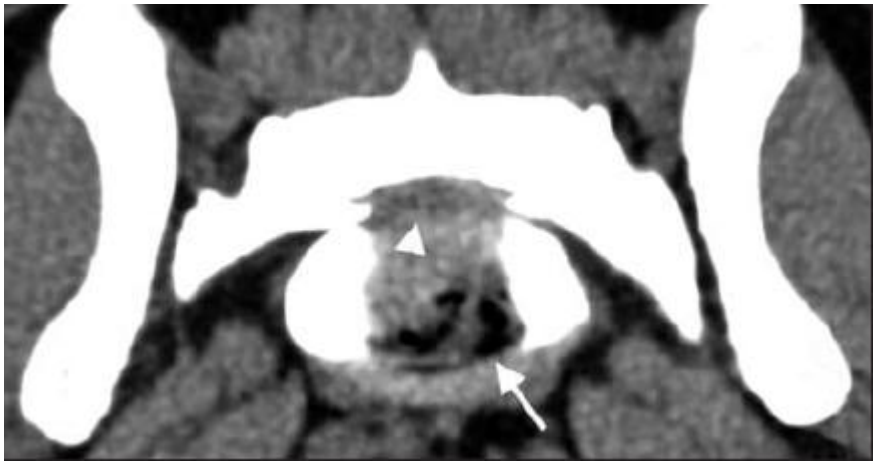
5.4.1.6. Linear Tomography

Linear tomography has been used to diagnose DLSS. It produces a detailed image of a single narrow plane within the body by obliterating the images of structures above and beneath it (Gibbs, 1973; Gaschen, Lang & Haeni, 1995; De Risio et al., 2000). It may also provide a more accurate evaluation of the position of the neural tissue when combined with epidurography (Ramirez & Thrall, 1998). Linear tomography requires specialised equipment and has essentially been replaced by cross-sectional imaging techniques such as CT or MRI (Lanz & Rossmeisl, 2012).

5.4.1.7. Computed Tomography

CT is a noninvasive cross-sectional imaging modality using x-rays, a detector that produces raw numerical data, and a computer system that converts raw data into images (Jones, Wilson & Bartels, 1994; De Risio et al., 2000). An advantage of CT over conventional radiography is that it has the ability to visualise lateral recesses, intervertebral foramina, articular process joints and the vertebral canal (Jones, Cartee & Bartels, 1995; Jones et al., 1996a; Sharp & Wheeler, 2005b). Inherent contrast provided by the epidural fat enables direct visualisation of individual nerve roots (Ramirez & Thrall, 1998). CT, however, does not permit differentiation between the nucleus pulposus and the annulus fibrosus of the intervertebral disc (Kärkkäinen, Punto & Tulamo, 1993). CT findings in dogs with DLSS include loss of epidural fat within the vertebral canal or intervertebral foramina, L_7-S_1 disc protrusion into the vertebral canal, presence of compressive soft tissues within the intervertebral foramina or vertebral canal, thecal sac displacement, vertebral subluxation, osteophytosis, sacral osteochondrosis, hypertrophy of the interarcuate ligament, and the vacuum phenomenon (figure 16) (Jones et al., 1996a; Jones et al., 2000a; Jones & Inzana, 2000b; Suwankong, Voorhout, Hazewinkel & Meij, 2006; Meij & Bergknut, 2010).

Figure 16 - Transverse CT image of the L_7-S_1 intervertebral disc in a dog. Note the intervertebral disc protrusion into the vertebral canal (arrowhead) and the vacuum phenomenon (arrow) (adapted from Suwankong et al., 2006).



Transverse, parasagittal and dorsal views are useful to assess L_7-S_1 intervertebral foramen involvement (Wood, Lanz, Jones & Shires, 2004). Contrast medium has been reported to hamper imaging interpretation, especially within the vertebral canal, by causing blooming and beam hardening artifacts associated with thecal sac contrast filling (Jones et al, 1996a). However, a correlation between lesions exhibiting CT enhancement and location of compressive tissues during surgery has also been reported. Because it is debated whether intravenous contrast-enhanced CT scans may facilitate the detection of compressive soft tissues within the vertebral canal, pre and post contrast-enhanced CT scans should be attained (Feeney, Evers, Fletcher, Hardy & Wallace, 1996; Jones et al., 1999). Positional CT is a suitable technique for quantifying dynamic changes in L_7-S_1 intervertebral foraminal morphology in dogs with DLSS and therefore may be useful tool in the detection of the disease. Foraminal compression and disc protrusion may be accentuated by extension of the spine (Jones et al., 2008). The possibility of three-dimensional reconstruction in CT may aid surgical planning and be a useful post-surgical tool (Meij, Voorhout & Wolvekamp, 1996; Jones et al., 2000a). When compared to MRI, CT is a much faster diagnostic imaging modality (Sharp & Wheeler, 2005b; Lanz & Rossmeisl, 2012). It also bears lower costs and better distinction of osteophytes, articular process joint disease, soft tissue calcification, and soft tissue gas opacities (Jones et al., 2000a). CT is often, however, less sensitive than MRI for discriminating soft tissues within the spinal canal and has the disadvantage of using ionising radiation (De Risio et al., 2000; Meij & Bergknut, 2010). Some CT abnormalities are clinically insignificant, especially in older dogs (Jones & Inzana, 2000b; Sharp & Wheeler, 2005b). If clinical signs consistent with DLSS are present, compression should be suspected

at the locations where there is an increase in perineural soft tissue opacity with absence of epidural fat (Ramirez & Thrall, 1998).

5.4.1.8. Magnetic Resonance Imaging

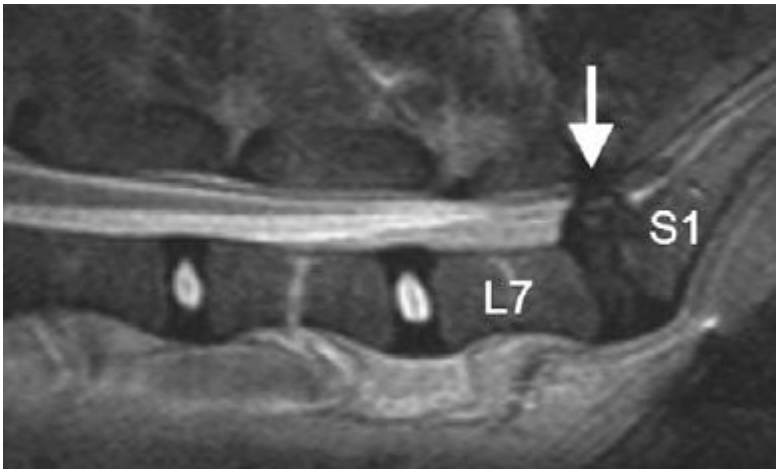
The interaction of atomic nuclei with magnetic properties and electromagnetic radiation and magnetic fields results in absorption and release of detectable levels of energy. This energy, through a computer assisted technique termed magnetic resonance imaging, may be used to construct a diagnostic anatomic image (Thomson et al., 1993). MRI provides a higher soft tissue resolution than CT, which makes it a better diagnostic imaging modality to observe the spinal cord and cerebrospinal fluid, detect ligamentous, radicular and intramedullary pathologies, and evaluate intervertebral disc anatomy and degeneration. MRI findings in dogs with DLSS are similar to those observed with CT. They include displacement or loss of epidural fat, disc protrusions, presence of soft tissues compressing the intervertebral foramina or vertebral canal, hypertrophy of the interarcuate ligament, articular process osteophytosis and fracture, and vertebral subluxation (Haan, Shelton & Ackerman, 1993; Adams, Daniel, Pardo & Selcer, 1995; Jones et al., 2000a; Mayhew, Kapatkin, Wortman & Vite, 2002). Intervertebral disc degeneration is characterised by a decreased T2 signal intensity within the nucleus pulposus due to loss of water content (figure 17) (Kärkkäiken, Mero, Nummi & Punto, 1991). Dynamic studies may be advantageous in the diagnosis of DLSS. In presence of clinical signs consistent with both lumbosacral disease and T_3-L_3 myelopathy, the diagnostic imaging technique of choice should be MRI, because it will allow visualisation of the entire vertebral column and spinal cord from T_2 to the sacrum without repositioning the patient (Lanz & Rossmeisl, 2012; Dewey, 2013). Stenosis of the L_7-S_1 intervertebral foramen may be best evaluated with parasagittal and transverse magnetic resonance images (Gödde & Steffen, 2007). MRI has the ability to obtain sagittal and dorsal plane images without degradation of the image due to reformatting and permits earlier detection of disc degeneration, which pose as advantages over CT. It requires more time than CT and is less widely available, but does not involve the use of ionising radiation (Ramirez & Thrall, 1998; De Risio et al., 2000; Sharp & Wheeler, 2005b). There is a high degree of agreement between CT and MRI findings in dogs with DLSS. The degree of agreement between diagnostic imaging and surgical findings appears to be lower (Suwankong et al., 2006), so confirmation of diagnosis should not rely solely on imaging findings (Sharp & Wheeler, 2005b).

5.4.2. Electrodiagnostic studies

Electromyography is the recording and study of insertional, spontaneous, and voluntary electric activity of muscle. In DLSS it is used to demonstrate abnormal spontaneous activity

in the muscles of the pelvic limbs, tail or perineum. In the pelvic limb, the most commonly used nerves are the sciatic-tibial nerve and the common peroneal nerve (Cuddon, 2002; Lanz & Rossmeisl, 2012).

Figure 17 - T2-weighted midsagittal MR image of the lumbosacral region of a dog. Note the presence of disc protrusion at the level of L7-S1 (arrow) and the loss of the nucleus pulposus water signal, indicating disc degeneration (adapted from Meij & Bergknut, 2010).



Electromyography may be helpful to differentiate subtle lesions as lower motor neuron or upper motor neuron in nature (Sharp & Wheeler, 2005a). Depending on the severity of the disease, motor and sensory nerve conduction studies may be normal or abnormal. The most sensitive and informative electrophysiologic studies for the evaluation of *cauda equina* compression are f-wave studies and somatosensory evoked potentials. F-wave studies evaluate motor pathways in the ventral nerve roots and the peripheral axons of motor and mixed nerves (Lanz & Rossmeisl, 2012). Somatosensory evoked potentials provide information about lesion location and sensory nerve root involvement. Latencies of tibial nerve lumbar somatosensory evoked potentials in dogs with DLSS may be prolonged and amplitude may be reduced, when compared to clinically normal dogs. Cortical evoked potentials have shown neurological abnormalities before presentation of neurological signs (Delamarter, Bohlman, Dodge & Biro, 1990; Meij, Suwankong, Van Dem Brom, Haagen & Hazewinkel, 2006). Dogs with compressive radiculopathy are also anticipated to have prolonged f-wave latencies. Electrophysiologic studies may provide diagnostic information complementary to clinical and diagnostic imaging examinations. Abnormal electrophysiologic test results are consistent with a lower motor neuron disorder in animals with DLSS, however, they are nonspecific for the cause (Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012). Concurrently, normal electrophysiologic studies have been reported in animals with clinical signs, diagnostic imaging and surgical findings consistent with DLSS (De Risio, Sharp, Olby, Muñana & Thomas, 2001; Tarvin & Lenehan, 2014). In electromyographic studies, before

concluding a muscle is normal, it should be tested at multiple sites and three different depths of needle insertion at each site (Sisson et al., 1992). Electromyography has the advantage of differentiating neurologic diseases from orthopaedic ones (De Risio et al., 2000). However, it involves special equipment and expertise to perform and evaluate, is time consuming, and requires general anesthesia for accurate studies to be performed (Cuddon, Murray & Kraus, 2003; Meij & Bergnut, 2010; Tarvin & Lenehan, 2014).

5.4.3. Force plate analysis

Force plate analysis (FPA) is a noninvasive method for measurement of ground reaction forces, thus evaluating human or animal locomotion (Suwankong et al., 2007). Reports on FPA have shown that pelvic limb propulsive forces in dogs with DLSS were lower than those of healthy dogs. Short and long-term outcome of dorsal laminectomy in dogs with DLSS has also been evaluated with FPA, revealing re-establishment of normal propulsive force of the pelvic limbs 6 months after surgery. FPA is an advantageous technique to detect gait alterations that may not be evident in visual observation alone (Van Klaveren et al., 2005).

5.5. Medical Treatment

For dogs experiencing their first episode of lumbosacral pain or whose pain is mild and intermittent, medical therapy, including confinement and administration of anti-inflammatory and analgesic medication, is often recommended. Nonsteroidal anti-inflammatory drugs, corticosteroids in anti-inflammatory dosages, and opioid analgesics are primary drugs used in the medical management of lumbosacral pain (Denny et al., 1982; Danielsson & Sjöström, 1999; De Risio et al., 2000). A period of 4 to 14 weeks of conservative treatment has been reported (Coates, 2004; De Decker, Wawrzenski & Volk, 2014). Neuropathic pain-modifying agents, such as gabapentin, amantadine, and pregabalin, are becoming more frequently used and can successfully manage pain in some cases of DLSS. If indicated, body weight reduction and physiotherapy in a water treadmill may aid in the conservative management of the disease (Meij & Bergknut, 2010; Dewey, 2013). An approximate success rate of 50% has been reported in dogs managed medically, with included animals showing improvement or resolution of clinical signs (Ness, 1994). Following confinement and medical treatment, long periods of rest and exercise restriction, often lasting several months, may be necessary for dogs to respond favorably (Sjöström, 2003; Lanz & Rossmeisl, 2012). Improvement is, nevertheless, often transient, because resumption of normal activity frequently elicits recurrence of clinical signs, especially in working dogs (Denny et al., 1982; Danielsson & Sjöström, 1999; Sharp & Wheeler, 2005b; Dewey, 2013). However, a long period of rest may be associated with a worse prognosis if neurological deficits develop during that time

(Sjöström, 2003; De Risio et al., 2000). Reports on epidural administration of methylprednisolone acetate have demonstrated improvement of clinical signs in 79% and total recovery in 53% of 38 dogs with DLSS associated with intervertebral disc lesions (Janssens, Beosier & Daems, 2009). This study, however, did not include animals with severe clinical signs, which makes it difficult to determine how effective it is in those cases. Although conservative treatment does not cure the underlying cause for DLSS, it may result in sufficient and adequate pain management (Meij & Bergknut, 2010).

5.6. Surgical Treatment

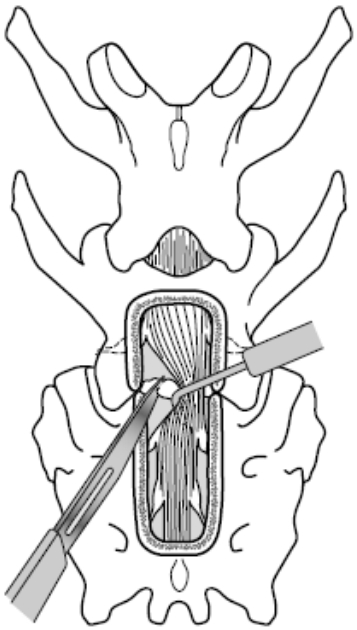
Surgical treatment of DLSS is indicated if neurological deficits and moderate to severe pain refractory to medical treatment are present. CT or MRI findings of increased soft tissue suggestive of epidural fibrosis, especially contrast-enhanced, are indications for surgery (Sharp & Wheeler, 2005b). The purpose of the surgery is to alleviate the compression of the conus medullaris or the nerve roots of the *cauda equina* that is causing clinical signs. The surgical technique most widely used is decompression by dorsal laminectomy. Distraction-fusion of L_7-S_1 has also been used alone or in combination with dorsal laminectomy to treat DLSS. Indications for distraction-fusion include a notably variable degree of compression between flexion and extension and subluxation of L_7-S_1, which suggest lumbosacral instability (Slocum & Devine, 1998; Danielsson & Sjöström, 1999; De Risio et al., 2000; Sharp & Wheeler, 2005b; Suwankong et al., 2007). Animals with uni or bilateral MRI findings and clinical signs consistent with foraminal stenosis have also been treated with lateral foraminotomy (Wood et al., 2004; Gödde & Steffen, 2007). Definitive criteria for surgical technique preference are lacking (Sharp & Wheeler, 2005b). Laminectomy alone has been reported to be ineffective in dogs with chronic incontinence (De Risio et al., 2001). Distraction-fusion alone may be insufficient for dogs with neurological deficits, severe pain, or chronic *cauda equina* compression (Slocum & Devine, 1998; Sharp & Wheeler, 2005b). Exploratory surgery may be necessary if clinical and other findings indicate DLSS but radiographic examination fails to demonstrate a lesion (Sjöström, 2003; Tarvin & Lenehan, 2014).

5.6.1. Dorsal laminectomy

A dorsal laminectomy removes the dorsal aspect of the spinal canal, which will relieve pressure on the nerve roots of the *cauda equina* and allow removal of the prolapsed disc material. It can be combined with foraminal decompression (foraminotomy), facetectomy or discectomy (Tarvin & Prata, 1980; De Risio et al., 2000; Sharp & Wheeler, 2005b). Cadaver studies have shown increased lumbosacral motion following dorsal laminectomy (Smolders et

al., 2012a; Early, Mente, Dillard & Roe, 2013). In vitro studies have reported that, when combined with discectomy, dorsal laminectomy causes decreased stiffness in ventroflexion and significant instability in all motion directions (Smolders et al., 2012b; Early et al., 2013). Surgical positioning is usual in ventral recumbency, with the pelvic limbs flexed and pulled forward, which will allow stretching of the dorsal annulus fibrosus, opening of the dorsal space between the laminae of L_7 and the sacrum, and therefore facilitate the access to the vertebral canal. Rongeurs can be used to remove the spinous process and laminae of $L_{7,}$ as well as the cranial part of the sacral spinous process (Sjöström, 2003; Lanz & Rossmeisl, 2012). To allow better identification and manipulation of the nerve roots, the dorsal surface of the sacrum may be removed caudally. If a high-speed burr is used, care must be taken because the laminae are thin, and the area should be irrigated with saline. In some cases, the spinous process of L_7 and the caudal portion of the median sacral crest may be left intact (Lanz & Rossmeisl, 2012). Bone removal should be cautious and as limited as possible, especially if the disease is secondary to lumbosacral instability. The removal of portions of discs and articular processes may further destabilise the spine and predispose to postoperative sequelae (Tarvin & Lenehan, 2014). Fracture of the articular process of L_7 can occur due to excessive bone removal after laminectomy (Adams et al., 1995, Moens & Runyon, 2002). Visual inspection for hypertrophy and dissection of the interarcuate ligament allows access to the spinal canal and provides decompression of the nerve roots. Manipulation of the interarcuate ligament must be careful not to damage the *cauda equina* (Sjöström, 2003). If disc protrusion occurs laterally, the caudal articular process of L_7 must be partially removed to identify and decompress the laterally attenuated roots. With the risk of destabilisation, the caudal articular process of L_7 and the cranial articular process of S_1 may be fully removed to allow total access to the L_7 nerve root. Inspection of the nerve roots can be performed with a blunt instrument. The L_7-S_1 foramen and L_7 nerve roots should be carefully inspected for signs of compression or adhesion that may be causing tethered cord syndrome (De Risio et al., 2000; Lanz & Rossmeisl, 2012). The dural sac should be identified and inspected for any signs of swelling or adhesions (Meij & Bergknut, 2010). Although some reports have suggested that facetectomy may cause few clinical problems in result of instability, this procedure should be avoided, if possible (Danielsson & Sjöström, 1999; Sjöström, 2003). A partial discectomy can be performed to further relieve compression. This procedure starts with fenestration (or annulectomy). In order to do so, the *cauda equina* is moved laterally to one side with the nerve hook retractor, and one half of the dorsal surface of the annulus fibrosus is removed with a scalpel blade (figure 18). The procedure is then repeated on the contralateral side to remove the remaining of the annulus fibrosus.

Figure 18 - Fenestration after dorsal laminectomy. The nerve roots are retracted bilaterally so that the annulus fibrosus can be removed (adapted from Johnson & Dunning, 2005).



The annulectomy is followed by a nuclear pulpectomy (or nucleotomy). The nucleus pulposus can be removed with Lempert or Kerrison rongeurs. Injury of the internal vertebral venous plexus will lead to hemorrhage, which will obscure vision of the *cauda equina* and foraminal area. Hemorrhage can be controlled with absorbable gelatin sponges. The laminectomy site is then covered with an autonomous fat graft, derived from the surrounding subcutaneous area to prevent peridural fibrosis and new bone formation and therefore provide spinal cord protection (Trevor, Martin, Saunders & Trotter, 1991; Quist et al., 1998; Sharp & Wheeler, 2005b; Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012; Dewey, 2013). Careful suturing of all layers is essential to prevent seroma formation and postoperative infection (Sjöström, 2003; Meij & Bergknut, 2010). Although it does not address instability if it is a contributing factor, laminectomy often provides rapid improvement of mild gait abnormalities, resolution of pain and minor neurological deficits (Danielsson & Sjöström, 1999; De Risio et al., 2001). Post-surgical prognosis seems to be poorer for animals with severe neurological deficits and chronic urinary or fecal incontinence prior to surgery (De Risio et al., 2000; Linn et al., 2003). Animals with chronic urinary incontinence of more than 1 month have a guarded prognosis when treated with laminectomy alone, therefore treatment should also include fixation and fusion (De Risio et al., 2001; Sharp & Wheeler, 2005b). Limitations to dorsal laminectomy are the fact that unless it is combined with foraminotomy, which may increase the risk of articular process fracture, it cannot relieve clinical signs of foraminal stenosis. In dogs with pelvic limb lameness it may be an inadequate choice of procedure, unless it can be proven that

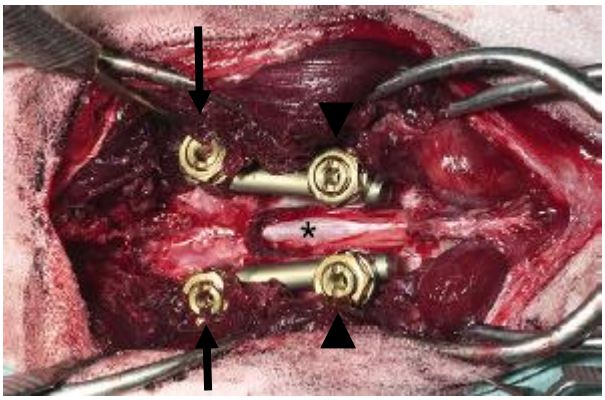
compression is at the level of the S1 nerve root (Jeffery, Barker & Harcourt-Brown, 2014). Formation of peridural fibrosis may also occur after dorsal laminectomy. Although it is not frequently reported in dogs, it is a source of pain in human patients (Robertson, 1996).

5.6.2. Distraction-fusion

Overriding and collapse of the lumbosacral joint cause exuberant tissue production which culminates in lumbosacral joint ankylosis. This contributes to further nerve root compression and intervertebral disc degeneration. Arthodesis of the lumbosacral joint interferes with the pathophysiological processes behind L_7-S_1 instability and prevents these phenomenons by opening the collapsed lumbosacral foramina and adding stability to the joint through the use of pins or screws. Distraction-fusion may be performed alone or combined with dorsal laminectomy, especially in dogs with severe pain, neurological deficits, or a large disc protrusion (Bagley, 2003; Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012). Surgical positioning is similar to that of the dorsal laminectomy technique. Distraction should not be excessive because it may increase pressure on the L_6-L_7 intervertebral disc and cause prolapse at that level. Distraction may be performed with a lamina spreader and should culminate in a correct anatomic alignment of the L_7-S_1 articular process joint (Lanz & Rossmeisl, 2012). The ends of the lamina spreader are placed one arm on the L_7 side and the other on the sacral side. The maximal distraction of the lamina spreader may not be sufficient to distract the lumbosacral articulations for anatomical reduction. The purchase points of the lamina spreader may need to be placed further laterally toward the articular processes to achieve desired distraction, if that is the case (Bagley, 2003). Then, the articular processes should be slightly overdistracted to facilitate removal of the articular cartilage, and placed back in their correct anatomical position. Fusion may be promoted with a cancellous bone graft harvested from the wing of the ilium or the dorsal spinous process of L_7 (in cases which a dorsal laminectomy has also been performed) and placed around the articular joint spaces to aid fusion. Cortical screws may be placed in a lag fashion and directed in a ventrolateral direction at a 30 to 45 degree angle in relation to the sagittal plane, extending from dorsomedial on the L_7 articular process to ventrolateral on the sacrum. Screws must not be too large or placed too tightly due to risk of fracture of the articular processes. To facilitate removal if needed, bone wax may be placed in the screw heads. Because of the proximity to the lumbosacral trunk, the drill hole for screw placement should not extend beyond the distal cortex of the sacrum (Bagley, 2003; Sharp & Wheeler, 2005b; Lanz & Rossmeisl, 2012). Fixation may also be achieved with an internal fixator such as polymethylmethacrylate, embedded in pin ends or screw heads (Fitzpatrick & Yeadon, 2008; Meij & Bergknut, 2010). Pedicle screw and rod

fixation has also been described to manage lumbosacral instability. In this technique, a cancellous bone graft is placed in the intervertebral disc space after nucleotomy and removal of the cartilaginous end plates. Then, titanium screws are placed and connected with contoured titanium rods (figure 19). This method avoids loading of the articular processes (Worth et al., 2009; Meij & Bergknut, 2010; Smolders et al., 2012c; Tellegen, Willems, Tryfonidou & Meij, 2015). Several techniques for surgical stabilisation of the lumbosacral joint are available. Besides the previously mentioned, an intervertebral distraction titanium bolt supplemented with pins, screws, and polymethylmethacrylate has also been reported (Fitzpatrick & Yeadon, 2008).

Figure 19 - Dorsal view of the lumbosacral region after dorsal laminectomy and pedicle screw and rod fixation. The screws are placed into the L_7 (arrows) and S_1 (arrowheads) pedicles and connected with titanium rods. Note the laminectomy defect (asterisk) (adapted from Meij & Bergknut, 2010).



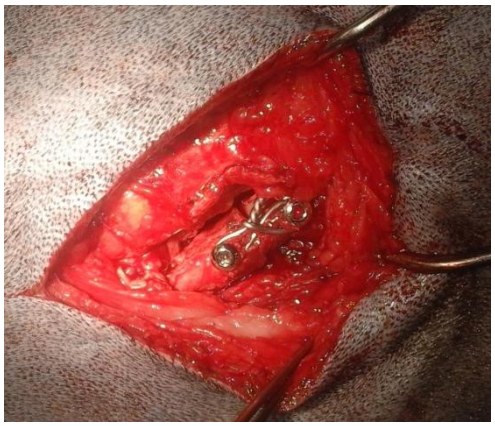
5.6.3. Lateral foraminotomy

If CT or MRI findings are consistent with foraminal stenosis, a foraminotomy may be performed (Meij & Bergknut, 2010). Findings such as loss of visualisation of normal epidural or periradicular fat within the foramen, increase of soft tissues within the foramen, occlusion of the foramen by laterally herniated discs, and articular process osteophytosis are consistent with lumbosacral radiculopathy (Adams et al., 1995; Jones et al., 1996a; Sharp & Wheeler, 2005b). Lateral foraminotomy may be used in combination with dorsal laminectomy. If so, bone dorsal to the foramen is removed, without removing the articular processes or connecting the foramen with the laminectomy site (Sjöström, 2003; Gödde & Steffen, 2007, Meij & Bergknut, 2010). Different techniques have been reported to address foraminal stenosis. An endoscopically assisted lumbosacral foraminotomy, involving a mini-dorsal laminectomy over the caudal portion of the L_7 lamina, and leaving the dorsal spinous process intact, has been described by Wood et al. (2004). Although it is a less destabilising technique to treat foraminal stenosis which proves to be effective in enlarging foraminal middle and entry zones, it did not provide expected enlargement of the exit zone. A transiliac approach

followed by endoscopical exploration of the intervertebral disc and foramen has also been described in cadavers. However, no clinical studies have been performed to evaluate its efficacy (Carozzo et al., 2008). A lateral foraminotomy via lateral approach has also been reported to achieve a good outcome in 8 of 8 treated dogs. This technique, however, has the disadvantage of not being able to grant access to the entrance zone of the lumbosacral foramen (Gödde & Steffen, 2007). A partial iliac osteotomy, with ventroflexion of the ilium, followed by lateral foraminotomy and corpectomy, in cases where there was concurrent intervertebral disc protrusion, has also been reported in 5 dogs. Stabilisation of the ilium was accomplished using a lateral bone plate or two screws and a tension-band cerclage wire (figure 20). Postsurgical CT scans at 6 months revealed absence of new bone formation at the foraminotomy sites and all animals had a good to excellent outcome (Saulnier-Troff & Motta, 2014).

Less invasive techniques to address DLSS may decrease post-surgical mobility and morbidity, avoid destruction of the articular processes, and involve less soft tissue and bony disruption. These may contribute to less postoperative instability (Wood et al., 2004). Advanced diagnostic imaging modalities have allowed a more accurate and focal localisation of the neurologic compression, which has been shown to occur, in many human cases, at the level of the intervertebral foramina, as well as central canal stenosis (Jenis & An, 2000).

Figure 20 - Dorsal view of the lumbosacral region after iliac osteotomy and L_7-S_1 foraminotomy. Two screws and a tension-band cerclage wire are used to stabilise the ilium (original image).



A study on MRI findings in 13 dogs with clinical signs of DLSS revealed that 54% had foraminal involvement. Foraminal involvement was reported as partial (1 dog) or complete foraminal occlusion (4 dogs) or intervertebral disc protrusion involving the foramen (2 dogs). In this study, two of the included animals had recurrence of pain 3 months after undergoing dorsal laminectomy. Although statistical relevance is debatable, it should be noted that both dogs had MRI findings consistent with partial and complete foraminal occlusion (Adams et al., 1995). A retrospective study on MRI and CT findings in 12 dogs surgically treated with

dorsal laminectomy revealed that 83% had foraminal stenosis on both CT and MRI. Postoperative CT scans revealed foraminal stenosis in all 12 dogs included in the study (Jones et al., 2000). In a review of lumbar failed back syndrome in human patients, lack of recognition or inadequate treatment of lateral canal stenosis was considered the cause of pain in 60% of patients (Burton, Kirkaldy-Willis, Yong-Hing & Heithoff, 1981). Therefore, the presence and severity of foraminal stenosis should be evaluated in dogs with clinical signs of DLSS and the chosen surgical approach should, if necessary, address it.

5.7. Postoperative care

Pain management and local application of cold packs may be used initially (Bagley, 2003; Meij & Bergknut, 2010). Confinement is advised for 3 to 4 weeks following surgery. This period is followed by exercise restriction with a gradual return to normal activity over a period of 6 to 8 weeks. Inadequate rest after surgery may risk a poor recovery. Working or highly active dogs are recommended an extra 3 to 4 weeks of transition before full work is resumed (De Risio et al., 2001; Sjöström, 2003). Distraction-fusion surgical technique reports have suggested strict rest until radiographic evidence of fusion is accomplished. A gradual return to normal activity, accompanied by physical therapy, leash walks, swimming, and use of underwater treadmills over a period of 2 to 3 months can improve long-term outcome (Bagley, 2003; Meij & Bergknut, 2010). In patients with affected urinary or fecal continence, adequate bladder care and prevention of fecal soiling of the perineal region may be necessary (Dewey, 2013). The patient should also be kept on clean and soft bedding (De Risio et al., 2000).

5.8. Outcome and prognosis

Although there are several reports in the literature of postoperative outcome of dorsal laminectomy and distraction-fusion, none have compared the outcome of the two techniques. Outcome of dorsal decompression for treatment of lumbosacral pain assessed by veterinary surgeons and owners ranges from good to excellent. In working dogs, these results are less favorable due to higher performance demands (Meij & Bergknut, 2010). Two studies in which dorsal laminectomy and discectomy were performed revealed good to excellent results in 77% and 73% after a mean follow-up time of 14 and 21 months, respectively (Oliver, Selcer & Simpson, 1978; Lanz & Rossmeisl, 2012). Tarvin & Prata (1980) reported the results of dorsal laminectomy, bilateral facetectomy, and foraminotomy, in 15 dogs with lumbosacral stenosis. The follow-up ranged from 13 months to 4 years and alleviation of clinical signs occurred in all cases. Another study on dorsal decompression revealed clinical improvement in 93% and a return to normal function in 79% of 131 treated dogs. In this study, follow-up

examination consisted in physical examination by the authors or telephone interview. Mean follow-up time was 26 months (5 to 73 months). Recurrence of clinical signs occurred in 18% of the dogs however, for most of these patients, the underlying cause was not found. Severity of clinical signs upon presentation seems to play an important part in postoperative prognosis (Danielsson & Sjöström, 1999). Another retrospective study revealed a substantial improvement of all clinical signs or full recovery in 78% of 69 dogs. Mean follow-up time was 38 (6 to 96 months) and examination was performed via telephone inquiry. Recurrence was reported in 3% of cases. In this study, the presence of urinary or fecal incontinence was considered a negative prognostic factor. Urinary incontinence of more than 1 month also appears to be indicative of a worse outcome (De Risio et al., 2001). In a study of 29 military working dogs, 41% had a full recovery and 38% showed clinical improvement. Recurrence rate was approximately 28%. Mean follow-up period was 24 months (2 to 82 months). Increasing age at surgery and severity or chronic progression of clinical signs were reported to be less favourable prognostic factors (Linn et al., 2003). A retrospective study of 156 dogs demonstrated improvement in 79%. Dogs undergoing dorsal laminectomy followed by discectomy showed significantly less improvement than those undergoing dorsal laminectomy alone. Mean questionnaire-derived follow-up period was approximately 25 months (3 to 60 months) (Suwankong et al., 2008). In a study using FPA, although owners were satisfied with the outcome of dorsal laminectomy, propulsive forces were only partially restored in dogs with DLSS (Van Klaveren et al., 2005; Suwankong et al., 2007). Recurrence of clinical signs may have several causes. Scar tissue and new bone formation have been reported in animals surgically treated with dorsal laminectomy. Instability of the lumbosacral joint may also be a contributing factor. Other orthopaedic conditions or unrelated neurological disorders, common in older animals, may mimic clinical signs associated with DLSS. Although Linn et al. (2003) reported otherwise, preoperative duration of clinical signs has also been reported to not influence patient outcome, with the exception of urinary incontinence (Danielsson & Sjöström, 1999; De Risio et al., 2001). Few studies have reported long-term postoperative outcome of foraminotomy, facetectomy, or distraction-fusion (Sjöström, 2003; Sharp & Wheeler, 2005; Lanz & Rossmeisl, 2012). A study on distraction-fusion alone reported a minimum follow-up period of 2 months in which all 14 surgically treated animals had a satisfactory outcome (Slocum & Devine, 1986). A study on the combination of distraction-fusion with dorsal laminectomy in 26 dogs reported a return to normal ambulation in 85% of treated patients in a postoperative period of 6 months (Hankin, Jerram, Walker, King & Warman, 2012). Another study on distraction-fusion and dorsal laminectomy revealed improvement in 76% of 17 dogs. Mean CT follow up was 12 months. In this study, screws

broke or were pulled out in 5 dogs and 2 dogs needed revision surgery (Golini, Kircher, Lewis & Steffen, 2014). In a retrospective study on dorsal laminectomy followed by pedicle screw-rod fixation in 12 dogs, 67% had resolution and 33% had improvement of clinical signs. Follow up-period ranged from 5 months to more than 4 years via owner questionnaires and was possible in 8 dogs. Recurrence of clinical signs occurred in 4 dogs (Tellegen et al., 2015). In humans, however, adjacent segment disease is an important concern and reported outcome of lumbar fusion in patients with DLSS (Guigui et al., 2000; Park, Garton, Gala, Hoff & McGillicuddy, 2004; Yang, Lee & Song, 2008). Although sometimes it causes no clinically relevant consequences, implant loosening, migration, and failure are risks of distraction-fusion techniques. It is usually a result of poor implant selection or suboptimal technique (Sharp & Wheeler, 2005b). Fracture of the articular process of L_7-S_1 and infection may also occur (Hankin et al., 2012; Lanz & Rossmeisl, 2012).

6. Case reports, case series and critical appraisals

Case reports and case series are, and have historically been, integral components of the veterinary medical literature. While new and more advanced research methods arise, paving the way for evidence-based medicine, evidence provided from case series and case reports has lost scientific significance, and its reliability, and therefore clinical acceptance, have been questioned (Nissen & Wynn, 2014; Garg, Lakhan & Dhanasekaran, 2016). When looking at many systems of hierarchical levels of evidence, case reports and case series remain low in the ranking, with systematic reviews representing the highest level of evidence (Albrecht, Werth & Bigby, 2009; JBI, 2014; Nissen & Wynn, 2014; Garg et al., 2016). The concepts of "case series" and "case reports" are not well defined in the literature. Therefore, the definitions proposed by Abu-Zidan, Abbas & Hefny (2012) in a study on the use of those concepts in the medical literature will be employed throughout this dissertation. Studies with four or less participants will be considered case reports and those with more will be considered case series. Although case series and case reports rank relatively low in the evidence hierarchy and have limitations such as lack of a control group, tendency to bias (similarly to other observational studies), and often incomplete data collection (especially when they are retrospective in conduct) (Albrecht et al., 2009; Kooistra, Dijkman, Einhorn & Bhandari, 2009), provided that they are adequately conducted and reported, are valuable tools in the detection of novelties which stimulate the generation of new hypotheses, support the emergence of new research, solve ethical constraints, and bare lower expenses when compared to more complex study designs (Gagnier et al., 2014; Nissen & Wynn, 2014; Garg et al., 2016).

Critical appraisal is the process of systematically examining research evidence to judge its trustworthiness, its value and relevance in a particular context (Burls, 2009). Poorly designed and conducted clinical trials can compromise the integrity of the research process and mislead healthcare decision-making at all levels (Moher, Schulz & Altman, 2001; Maskhar et al., 2009). Some areas of veterinary medicine have a large body of high ranking evidence, while many others only have poor and low quality forms of evidence (Schulz, Cook, Kapatkin & Brown, 2006; Dean, 2013). Therefore, a critical appraisal of available research is essential to make informed decisions in clinical practice. Concern has been raised about the need for better designed and reported clinical trials to assess the outcomes of surgical treatment of DLSS (Worth et al., 2009; Meij & Bergknut, 2010; Jeffery, 2014), which further emphasises the importance of a critical appraisal of published studies on the topic.

II. Aims

The aim of this study was to critically appraise the literature reporting the results of surgical treatment of DLSS; to identify gaps in current knowledge and ensure there is justification for future research on the subject; and finally, to propose study characteristics that would enrich the conduct and report of these studies.

III. Methods

1. Literature search

The search strategy was performed on July 2016 and included the use of three electronic databases: PubMed, Web of Science (1900-present), and Google Scholar (1900-present). Electronic search in PubMed and Web of Science was performed in English and in Google Scholar in Portuguese. Each search had similar components searched as keywords and medical subject headings joined using Boolean operators (Annex 1). The electronic search was complemented with a hand-search in references of review articles and book chapters by: Bagley (2003), Sjöström (2003), Sharp & Wheeler (2005b), Meij & Bergknut (2010) and Lanz & Rossmeisl (2012).

2. Inclusion and exclusion criteria

Case series or higher-ranking evidence was included. For inclusion, papers had to be in vivo studies which reported surgical outcomes of DLSS, published in peer-reviewed journals, with the full-text available in English or Portuguese. Articles also had to have at least 5 participants

and concern domestic dogs. Articles which reported only lumbosacral traumatic lesions, dyscospondylitis, osteochondrosis, or neoplasia, were excluded.

3. Screening process

All electronic references were imported into Endnote and all duplicates were removed. Articles that did not meet the inclusion criteria or met the exclusion criteria were assessed first by their title and secondly by their abstract, and were removed. The full text was then obtained, if possible. Articles were accessed through the internet if access was available from the Faculty of Veterinary Medicine of the University of Lisbon. If an article was unavailable online or at the Faculty of Veterinary Medicine Library, an attempt to retrieve it by electronic contact with the publishing journal was made.

4. Critical appraisal

A critical appraisal tool for case series combining the JBI critical appraisal checklists for case reports and case series (2016), the case report guidelines (Gagnier et al., 2014) and the three-minute critical appraisal checklist (Chan & Bhandari, 2011), was designed. The critical appraisal tool examines the conduct and reporting of the participant selection process, participant demographics and clinical information, condition measurement, surgical intervention, outcome assessment, and clinical practice guidance (Annex 2).

Clear criteria were considered when inclusion and exclusion criteria were described in detail in the case series. An unclear reporting of inclusion or exclusion criteria was considered when one or both of them were not reported. Criteria for inclusion or exclusion of participants for each study were also recorded. Consecutive inclusion of participants was considered when the authors clearly reported that all the patients presented in a certain time period were included in the study. If a specific time period was described but a clear mention that all patients presented in that time were included lacked, this was considered as “unclear”. Clear reporting of participant demographics was considered when age, breed and sex were reported for all included animals. Clear reporting of clinical information of the participants was considered if prevalence and duration of clinical signs were stated. Measurement of the condition was considered reliable if all animals were diagnosed with the same measure which assured its repeatability. If there was evidence of lack of standardisation in condition measurement between participants, the answer was registered as “no”. In lack of a validated diagnostic methodology for the diagnosis of DLSS, all diagnostic methods that can provide a diagnosis for DLSS were considered valid. When radiography was performed alone, and no confirmation of diagnosis was performed at surgery, the methodology was considered invalid.

Ancillary diagnostic investigations and pain elicitation maneuvers used for the diagnosis of DLSS were recorded. A clear description of the intervention was considered when the surgical procedure was fully described. A clear reporting of outcomes or follow-up results was considered when presence or absence of postsurgical clinical signs was fully described, as well as how and when follow-up was performed and measured. The reporting and measurement methodology for outcome assessment was registered, as well as study follow-up rates. It was considered that the case series provided takeaway lessons when it offered clinical practice guidance.

A summary of key criteria to answer the critical appraisal tool questions is presented in table 1.

The results of the critical appraisal were then collated into a summary table and analysed.

III. Results

1. Search and screening process

143 papers were initially identified. Following screening, 115 studies were excluded on title and abstract basis. 11 papers were then excluded due to inability to retrieve from the library. Finally, 17 papers fulfilled the inclusion criteria (figure 21).

2. Critical appraisal

The results of the close-ended questions of the critical appraisals are summarised in table 2. Table 3 summarises the results of the open-ended questions.

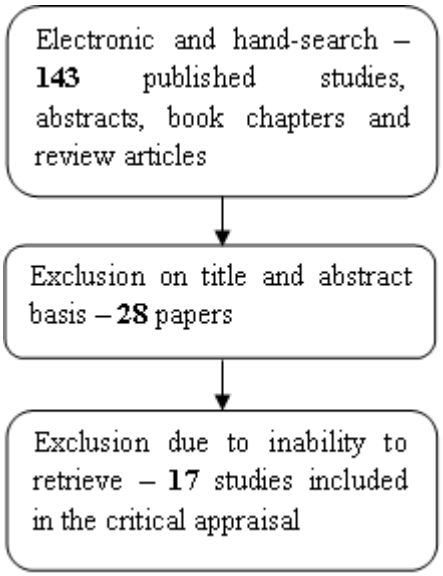
2.1. Were there criteria for inclusion and exclusion in the case series?

In 1 study (6%), it was considered that there were clear inclusion and exclusion criteria. In 16 studies (94%), it was unclear whether criteria for inclusion and exclusion of patients were applied. 47% of included studies (8 studies) did not clearly report any criteria, 12% (2 studies) clearly reported inclusion criteria, and 47% (8 studies) clearly reported exclusion criteria. Out of all the studies that reported exclusion criteria, 38% (3) of studies excluded animals with lumbosacral disease other than DLSS or concurrent orthopaedic problems. 25% excluded animals with LS disease other than DLSS alone and 13% excluded animals with orthopaedic problems alone. The remaining studies (2) had other exclusion criteria.

Table 1 - Key criteria to answer each question of the critical appraisal tool.

Question	Criteria
1 - Were there criteria for inclusion and exclusion in the case series?	Inclusion and exclusion criteria were described in detail
2 - Did the case series have consecutive inclusion of participants?	All patients presented in a specific time period were included in the study
3 - Was there clear reporting of the demographics of the participants in the study?	Age, breed, and sex of all participants was clearly reported
4 - Was there clear reporting of clinical information of the participants?	Duration and prevalence of clinical signs was fully reported
5 - Was the condition measured in a standard and reliable way for all participants included in the case series?	The condition was measured with the same instruments and in a reproducible way for all participants
6 - Were valid methods used for identification of the condition for all participants included in the case series?	A methodology that can provide a diagnosis of DLSS was used
7 – Was the intervention or treatment procedure clearly described?	The intervention was described in detail
8 – Were the outcomes or follow-up results of cases clearly reported?	Presence or absence of postsurgical clinical signs was fully described, as well as how and when it was assessed
9 – Does the case series provide takeaway lessons?	The study provided practical clinical guidance for readers

Figure 21 - Results of search and screening processes used to identify relevant papers.



2.2. Did the case series have consecutive inclusion of participants?

In 29% of studies (5 studies), consecutive inclusion of participants was reported. In 71% (12 studies) of included studies, it was unclear whether inclusion of participants was consecutive or not.

2.3. Was there clear reporting of the demographics of the participants in the study?

Age, breed, and sex, of the participants were clearly reported in 94% of studies (16 studies). In one study (6%), breed was not reported.

2.4. Was there clear reporting of clinical information of the participants?

It was considered that 35% (6) of studies clearly reported the clinical information of participants and 65% (11) did not.

2.5. Was the condition measured in a standard and reliable way for all participants included in the case series?

In 24% of studies (4 studies), it was considered that the condition was measured in a standard and reliable way, and in 76% of included studies (13 studies), it was not. When considering time of publication, particularly studies from the last 16 years, we can observe that 30% of studies had a standard and reliable diagnostic methodology.

2.6. Were valid methods used for identification of the condition for all participants included in the case series? Which methods were used?

It was considered that 94% (16) of included studies used valid methods for the identification of the condition. However, 6% (1) did not. Radiography was used in 88% of included studies, myelography in 53%, epidurography in 35%, discography in 29%, CT in 29%, MRI in 53%, transosseous vertebral venography in 12%, and electromyography in 18%. When considering studies from the last 16 years, it was observed that 29% and 90% of studies used CT and MRI, respectively, as a diagnostic tool for DLSS. However, considering the same time period, we can also observe that in only 30% of these studies the diagnostic methodology was standard and reliable. 82% (14) of studies reported how pain was elicited and 18% (3) did not mention how pain was elicited.

2.7. Was the intervention or treatment procedure clearly described?

The surgical technique was considered to be clearly described in 53% (9) of included studies and in 47% (8) it was not.

Table 2 – Summary of appraisal of the 17 studies which met the inclusion criteria (close-ended questions)

Article	Critical appraisal tool question*								
	1	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**
Oliver et al. (1978)	Unclear	Yes	Yes	No	No	Yes	No	No	Yes
Tarvin & Prata (1980)	Unclear	Unclear	Yes	Yes	No	Yes	No	No	Yes
Denny et al. (1982)	Unclear	Unclear	Yes	No	No	Yes	Yes	No	Yes
Slocum & Devine (1986)	Unclear	Unclear	No	No	Yes	No	Yes	Yes	Yes
Watt (1991)	Unclear	Yes	Yes	No	No	Yes	No	Yes	Yes
Ness (1994)	Unclear	Yes	Yes	No	No	Yes	No	Yes	Yes
Danielsson & Sjöström (1999)	Unclear	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes
Jones et al. (2000a)	Unclear	Unclear	Yes	No	Yes	Yes	No	Yes	Yes
De Risio et al. (2001)	Yes	Unclear	Yes	Yes	No	Yes	No	Yes	Yes
Linn et al. (2003)	Unclear	Unclear	Yes	No	No	Yes	No	Yes	Yes
Steffen et al. (2004)	Unclear	Unclear	Yes	No	No	Yes	Yes	Yes	Yes
Gödde & Steffen (2007)	Unclear	Unclear	Yes	Yes	Yes	Yes	Yes	Yes	Yes
Suwankong et al. (2007)	Unclear	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes
Suwankong et al. (2008)	Unclear	Unclear	Yes	Yes	No	Yes	No	Yes	Yes
Hankin et al. (2012)	Unclear	Yes	Yes	No	No	Yes	Yes	Yes	Yes
Golini et al. (2014)	Unclear	Yes	Yes	No	Yes	Yes	Yes	Yes	Yes
Tellegen et al. (2015)	Unclear	Unclear	Yes	No	No	Yes	Yes	Yes	Yes

*1- Were there criteria for inclusion and exclusion in the case series?; 2- Did the case series have consecutive inclusion of participants; 3- Was there clear reporting of the demographics of the participants in the study?; 4- Was there clear reporting of clinical information of the participants?; 5- Was the condition measured in a standard, reliable way for all participants included in the case series?; 6- Were valid methods used for identification of the condition for all participants included in the case series?; 7– Was the intervention or treatment procedure clearly described?; 8– Were the outcomes or follow-up results of cases clearly reported?; 9– Does the case series provide takeaway lessons?

Table 3 - Summary of appraisal of the 17 studies which met the inclusion criteria (open-ended questions)

Article	Critical appraisal tool question*			
	Criteria	**Methods**	**Outcomes**	**Post-discharge follow-up rate**
Oliver et al. (1978)	Exclusion	Radiography, TSV, EMG	PS	77% at different follow-up periods
Tarvin & Prata (1980)	Unclear	Radiography, TSV, myelography	PS	100% at different follow-up periods
Denny et al. (1982)	Unclear	Radiography	PS	100% at different follow-up periods
Slocum & Devine (1986)	Unclear	Radiography	PS by physical examination, radiography	100% at 2 months
Watt (1991)	Unclear	radiography, myelography, epidurography	PS by physical examination, OA	100% at 14 days
Ness (1994)	Unclear	radiography, myelography, epidurography	PS, OA	94% at different follow-up periods
Danielsson & Sjöström (1999)	Exclusion	radiography, myelography epidurography, discography	PS by physical examination, OA, OQ	100% at different follow-up periods
Jones et al. (2000a)	Exclusion	radiography, CT, and MRI	PS by PSE, CT	100% at 6 months
De Risio et al. (2001)	Exclusion and inclusion	radiography, EMG, myelography epidurography, discography, CT, MRI	PS by physical examination, OA, OQ	100% at different follow-up periods
Linn et al. (2003)	Exclusion	radiography, EMG, myelography, epidurography, discography, CT, MRI	PS by physical examination	100% at different follow-up periods
Steffen et al. (2004)	Unclear	radiography, myelography, discography, MRI	PS by physical examination, OA	100% at different follow-up periods
Gödde & Steffen (2007)	Exclusion	MRI	PS by physical examination, OA	100% at 6 months
Suwankong et al. (2007)	Exclusion	radiography, CT, MRI, FPA	PS by OA, OQ, FPA	100% at 6 months
Suwankong et al. (2008)	Exclusion	radiography, myelography, epidurography, discography, CT, MRI	PS by physical examination, OA, OQ	67% at different follow-up periods
Hankin et al. (2012)	Unclear	radiography, myelography, CT	PS by physical examination, radiography, OA, OQ	81% at 6 weeks
Golini et al. (2014)	Inclusion	MRI	PS by physical examination, CT	100% at different follow-up periods
Tellegen et al. (2015)	Unclear	radiography, CT, MRI, FPA	PS by OA, OQ, radiography, CT, FPA	58% at 4 to 6 weeks

*Critical appraisal tool questions: Criteria - Which criteria were used?; Methods - Which methods were used?; Outcomes - How were outcomes reported and measured?; Key to table: Post-discharge follow-up rate - What was the follow-up rate of the study?; TSV – Transossesous vertebral venography; EMG – electromyography; CT – Computed tomography; MRI – Magnetic resonance imaging; FPA – Force plate analysis; PS – postsurgical signs; OW – Owner assessment; PSE – Performance in standardised exercises; OQ – Owner questionnaire

2.8. Were the outcomes or follow-up results of cases clearly reported? How were outcomes reported and measured?

The outcomes of cases were considered to be clearly reported in 82% (14) of included studies. In 18% (3) of studies, it was unclear if outcomes were assessed by the owners or the veterinarian. In all included studies, outcomes were measured as presence or absence of postsurgical signs. In 59% (10) of these, postsurgical signs were measured by post-discharge physical examination of the participants. Out of the studies which reported outcome as postsurgical signs and in which there was no report of a post-discharge physical examination, 43% (3) did not report how outcomes were assessed and 29% (2) used owner questionnaires. Owner assessment was performed in 59% (10) of all included studies. In 60% of these (6), a standardised questionnaire was used. In the remaining (4) studies the method for owner assessment was not clearly specified. Objective outcome measurements, such as diagnostic imaging techniques, FPA, or performance in standardised exercises, were used in 35% (6) of the included studies. Out of these, 33% (2) used FPA, 83% used diagnostic imaging techniques (radiography or CT), and 17% (1) used performance in standardised exercises. In 65% (11) of included studies, objective measures of outcome were not reported.

2.9. Does the case series provide takeaway lessons?

All of the included studies provided takeaway lessons.

2.10. What was the follow-up rate of the study?

In 41% (7) studies, the follow-up rate at standard periods for at least one outcome measure was reported or possible to calculate from available data. The mean follow-up rate in these studies was 91%. Out of these studies, 57% (4) reported outcome assessment 1 year post-surgery with a mean follow-up rate of 37%. In 59% of included studies (10), the follow-up rate was reported or possible to calculate from available data, however, participants had different times of follow-up for all outcome measures. The mean post-discharge follow-up rate in these studies was 94%. The minimum time of outcome assessment between all included studies ranged from immediately post-surgery to 1,5 years.

IV. Discussion

1. Critical appraisal

1.1. Were there criteria for inclusion and exclusion in the case series? Which criteria were used?

Clear criteria for inclusion and exclusion of participants in a case series are essential for readers to be able to apply the series to their patients and help define the patients who have received the intervention and those who should not receive it (Albrecht, Werth & Bigby, 2009). In order for case series to be comparable against one another, clinical inclusion and exclusion criteria need accurate and clear reporting (Jeffery, 2014). Only one of the studies (6%) included in the critical appraisal clearly reported the criteria for inclusion and exclusion of participants in the case series. 47% of studies did not clearly mention any selection criteria. Although 47% of studies clearly reported exclusion criteria, only 12% reported inclusion criteria. Many studies reported as such: "10 dogs surgically treated for DLSS were included"; although these mention "inclusion", this reporting method does not clearly state that those were the criteria for inclusion, nor that all animals treated for DLSS were included in the study. Out of all the studies that reported exclusion criteria (8), 38% excluded animals with lumbosacral disease other than DLSS (discospondylitis, neoplasia, traumatic injuries) or concurrent orthopaedic problems. One study excluded only participants with concurrent orthopaedic problems. Comparison of treatments results between studies of these two types of criteria may be debatable because the second may have included patients which wouldn't have been included by the first. Many different terms are used in the literature to report lumbosacral disease, and it involves diverse pathological events (Denny et al., 1982; Watt, 1991; Danielsson & Sjöström, 1999; Sjöström, 2003; Lanz & Rossmeisl, 2012), which further highlights the importance of clear inclusion and exclusion criteria of participants in case series which report surgical treatment of the disease.

1.2. Did the case series have consecutive inclusion of participants?

29% of included studies clearly reported consecutive inclusion of participants. Case series are, due to their non-randomised nature, very prone to different kinds and risks of bias, especially selection bias (Green et al., 2011). Selection bias occurs not only when the selection of patients is not random but also if not all patients presenting with a relevant condition are included in order of entry (consecutive) (Lijmer et al., 1999). Therefore, consecutive inclusion of participants is highly relevant in case series. It increases their reliability and credibility, and reduces selection bias (Albrecht et al., 2009; The Joanna Briggs Institute (JBI), 2016b).

1.3. Was there clear reporting of the demographics of the participants in the study?

A full description of participant demographic information is essential to characterise the generalisability of research findings in a study and to make comparisons in replications, literature reviews or secondary data analyses (Sifers, Puddy, Warren & Roberts, 2002; JBI, 2016b). The majority of studies (94%) clearly reported age, breed, and sex, of the participants. These demographics were considered to be highly relevant because they provide valuable information on disease predisposition and prognostic factors. In studies on dogs with DLSS these seem to be particularly important due to the apparent predisposition of young adult, male, and large-breed dogs, especially German Shepherd dogs, to this disease (Danielsson & Sjöström, 1999; Linn et al., 2003; Lanz & Rossmeisl, 2012). Weight (Gödde & Steffen, 2007; Tellegen et al., 2015) and level of activity (Danielsson & Sjöström, 1999; DeRisio et al., 2001) were additionally reported in some of the included studies. A high level of activity has been reported as a risk factor for the development of DLSS and may play a role in patient prognosis (Ness, 1994; Jones et al., 1996b; Jones et al., 2000a; Linn et al., 2003; Sharp & Wheeler, 2005b; Worth et al., 2009), which highlights its importance in the reporting of patient demographics in case series. Weight may also play a part in DLSS and on patient prognosis, so it is also relevant to report (Worth et al., 2009).

1.4. Was there clear reporting of clinical information of the participants?

It is essential that all clinical information of the participants is clearly and fully reported (Green & Johnson, 2006; Albrecht et al., 2009; JBI, 2016b). Duration of clinical signs was a criterion for clear reporting because although some studies have found no correlation between duration of clinical signs and patient prognosis (Danielsson & Sjöström, 1999), some clinical signs of chronic progression have been associated with a negative prognostic value for post-surgical outcome (De Risio et al., 2001; Linn et al., 2003). Prevalence of clinical signs was also analysed because it is important to fully characterise the disease severity of all participants and the generalisability of the treatment results (Jaeschke et al., 1994; Lijmer et al., 1999). 65% of included studies did not clearly report duration and presence of clinical signs among the participants. This further hampers with a full and in-depth characterisation of the disease and jeopardises the investigation of causality between the chronicity of clinical signs and patient prognosis.

1.5. Was the condition measured in a standard and reliable way for all participants included in the case series?

It is important that the method of measurement of the condition is the same for all patients (standard) and produces repeatable and reproducible results (reliable) (Jaeschke, Guyatt & Sackett, 1994; Lijmer et al., 1999; JBI, 2016b). Measurement of the condition was considered standardised and reliable in as few as 24% of the appraised studies. However, when considering time of publication, particularly studies from the last 16 years, we can observe that 30% had a standard and reliable diagnostic methodology. This may reveal a trend towards a more cautious condition measurement in studies on the surgical treatment of DLSS over time. Standardisation and reliability should, however, not be mistaken for study quality. For example, in the study by Slocum & Devine (1986), the diagnosis relied on the signalment, physical examination, and radiographic findings of all included animals. Therefore, it was considered that this study was measured in a standard and reliable way. In the study by Suwankong et al. (2007), diagnosis relied on signalment, physical examination, radiography, and CT or MRI findings of included animals. Because not all included animals were diagnosed using the same methods, this study was not considered to have a standardised methodology. Now, unlike conventional radiography, CT and MRI have proven to be sensitive and specific detectors of *cauda equina* compression in dogs (Jones et al., 1995; Jones et al., 1996a; Ramirez & Thrall, 1998; Sharp & Wheeler, 2005b; Meij & Bergknut, 2010; Dewey, 2013). Although in one study (Slocum & Devine, 1986) the measurement of the condition was performed in a standard and more reliable way, the other (Suwankong et al., 2007) used far more accurate and advanced diagnostic imaging techniques, factors that make their quality incommensurable.

1.6. Were valid methods used for identification of the condition for all participants included in the case series? Which methods were used?

It is essential that a diagnosis is made based on existing definitions or diagnostic criteria. Outcome assessment validity depends on the use of validated condition measurement tools (Albrecht et al., 2009; JBI, 2016b). Because there is not a validated diagnostic methodology for the diagnosis of DLSS, all the diagnostic tools that have proven successful for the diagnosis of DLSS were considered valid. Although it has been reported that some abnormal radiographic findings are not exclusive or indicative of *cauda equina* compression (Morgan & Bailey, 1990; Mattoon & Koblik, 1993; McKee, 1993; Sjöström, 2003; Steffen et al., 2007; Meij & Bergknut, 2010), methodologies that used radiography alone as a diagnostic imaging modality were considered valid when surgical confirmation of DLSS was also performed. The

majority of studies (94%) used valid methods for the identification of the disease. However, the study by Slocum & Devine (1986) (accounting for 6% of studies) did not. This study used radiography alone as a diagnostic imaging tool and surgical confirmation of DLSS was not reported. That may be because distraction-fusion was the employed surgical technique, which may not allow for surgical detection of *cauda equina* compression. Although normal radiographic findings do not exclude DLSS (Morgan & Bailey, 1990; Ramirez & Thrall, 1998; Scharf et al., 2004; Steffen et al., 2007), radiography was used in 88% of studies, which further emphasises that it is commonly used in the diagnosis of DLSS. This may be because it is a fairly inexpensive procedure, when compared to CT or MRI, which can aid in the exclusion of diseases other than DLSS that may mimic its clinical signs (Morgan & Bailey, 1990; Mattoon & Koblik, 1993; McKee, 1993; Sjöström, 2003; Steffen et al., 2007; Meij & Bergknut, 2010). Although CT and MRI were used, respectively, in 29% and 53% of all included studies, when considering only studies from the last 16 years, those values are severely altered. Considering that time period, it was observed that 70% and 90% of studies used CT and MRI, respectively, as a diagnostic tool for DLSS. This further supports the premises that CT and MRI have become increasingly available and valuable diagnostic imaging tools both in the diagnosis of DLSS and in veterinary medicine (Ramirez & Thrall, 1998; Meij & Bergknut, 2010; Dewey, 2013). In a review article by Jeffery (2014), concern was raised about the quality of reporting of pain evocation methods used in studies on patients with DLSS. Therefore, pain evocation was also analysed in the 17 included studies. It was concluded that 82% of studies reported how lumbosacral pain was elicited, which demonstrates that the reporting quality of that measure is significant.

1.7. Was the intervention or treatment procedure clearly described?

A complete treatment protocol should be clearly described, so that it can be understood by the reader and replicated (Green & Johnson, 2006; JBI, 2016a). Although the majority (53%) of included studies described the surgical procedure in detail, 47% did not. Studies that did not fully describe the procedure often limited the reporting to: “as described by”; which does not comprise individual procedure differences that may have been performed and may interfere with patient outcome. For example, extent of the laminectomy (Adams et al., 1995, Moens & Runyon, 2002) and placement of a fat graft on the laminectomy site (Trevor, Martin, Saunders & Trotter, 1991; Quist et al., 1998; Sharp & Wheeler, 2005b; Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012; Dewey, 2013) may be important prognostic factors, and should, therefore, along with other procedure details, be fully and clearly described in a case series. Because, unlike the other items on the checklist, no specific criteria for clear reporting of the surgical

procedure were established, this evaluation is highly subjective, and therefore may be lead by bias. However, the results provide evidence that more detail than "as described by" is necessary in a case series, and that a complete and accurate reporting of the surgical technique is needed to demonstrate reproducible results.

1.8. Were the outcomes or follow-up results of cases clearly reported? How were outcomes reported and measured?

It is extremely important that the full clinical condition of the participants after an intervention or treatment is clearly reported (Green & Johnson, 2006; JBI, 2016b). In 82% of included studies, it was considered that this was adequately performed. Reporting of presence or absence of postsurgical signs is essential to fully characterise the success of an intervention. So that outcomes of different interventions can be compared and generalisation is possible, reporting of how and when follow-up was performed and measured is equally important. Although some studies which did not report postsurgical complications were classified as having a clear reporting methodology of follow-up results, this feature is also relevant in case series. In all included studies, outcomes were measured as presence or absence of postsurgical signs. In 59% of these, postsurgical signs were measured by post-discharge physical examination of the participants. Out of the studies reporting outcomes as postsurgical signs and in which there was no report of a post-discharge physical examination, 43% did not report how outcomes were assessed and 29% used owner questionnaires. The diagnosis of DLSS should be based on, among other factors, the physical examination of the animal (Sharp & Wheeler, 2005b; Meij & Bergknut, 2010; Lanz & Rossmeisl, 2012). Therefore, characterisation of the postsurgical condition of the treated animals should also rely on physical examination by an experienced professional.

Owner assessment was performed in 59% of all included studies. In 60% of these, a standardised questionnaire was used. However, not all studies using this outcome assessment measure provided a detailed description of the content of the questionnaires, which is desirable when clear and replicable outcome reporting and assessment methods are intended. In the remaining (4) studies the method for owner assessment was not clearly specified. Although subjective methods such as owner questionnaires and veterinary lameness scores have been validated and are useful outcome measures, they are a source of assessor bias. Therefore, a caregiver placebo effect by both veterinarians and pet owners should be considered when interpreting reports of patient response to treatment (Conzemius & Evans, 2012; Da Costa, 2014). However, there are currently no validated and specific owner questionnaires or veterinary lameness scores for outcome assessment of animals treated for

DLSS, which poses as a limitation to this kind of method. Objective outcome measures are valuable in improving the understanding of treatment effects in research studies, and provide results that are comparable between studies (Jeffery, 2014). These measures, which include diagnostic imaging techniques, FPA, or performance in standardised exercises, were used in 35% of the included studies. Out of these, 33% used FPA, 83% used diagnostic imaging techniques (radiography or CT), and 17% used performance in standardised exercises. Although they are valuable tools to assess screw position and condition and bone fusion in distraction-fusion techniques (Golini et al., 2014; Tellegen et al., 2015), significant association between imaging studies and postoperative outcomes has not been identified (Jones et al., 2000). Furthermore, there is also apparently no correlation between imaging findings and disease severity (Mayhew et al., 2002; Dewey, 2013).

1.9. Does the case series provide takeaway lessons?

Case series should provide clinical practice guidance for readers when presented with a similar case, so a summary of the key lessons learned from a case is essential (JBI, 2016a). All of the included studies provided takeaway lessons and, therefore, clinical practice guidance for readers.

1.10. What was the follow-up rate of the study?

Loss of patients to follow-up is important because it influences the validity of the treatment or study protocol (Chan & Bhandari, 2011). Due to an unclear reporting of follow-up at different times, it was challenging to assess follow-up rates of many of the included studies. In 41% of included studies, the follow-up rate was reported or possible to calculate from available data at standard periods for at least one outcome measure. The mean follow-up rate in these studies was 91%. Although follow-up was performed in standard times for each study, this did not happen between studies, so the follow-up rate was calculated at the time of the first outcome measurement. Presentation of this data as a mean rate for the first outcome measure alone, and not the entire time of follow-up assessment, results in an overestimation of the follow-up rate, which must be considered when interpreting this data. Conversely, because only some of the studies included in this category used standard periods of outcome measurement alone, this value could also be underestimated for studies which also reported outcomes at different times. In 59% of included studies, the follow-up rate was reported or possible to calculate from available data, however, participants had different times of follow-up for all outcome measures. The mean post-discharge follow-up rate in these studies was 94%. This value is higher than the follow-up rate of studies in which outcome assessment was performed at standard periods (91%), however, interpretation of this data must be careful, and comparison

is debatable. The minimum time of outcome assessment between all included studies ranged from immediately post-surgery to 1.5 years, which further emphasises the heterogeneity of included studies. As demonstrated, follow-up rates of studies on the surgical treatment of DLSS are apparently high, however, when looking at studies which assessed long-term outcome (more than 1 year) in standard periods (4 studies), the mean follow-up rate is as low as 37%. Although the hardship for a clear reporting of follow-up rates and periods for retrospective studies with a high number of participants is comprehensible, that method assures that comparison between treatment results and generalisation of findings are possible, and that a full interpretation of treatment results is feasible.

2. Limitations

This critical appraisal was hampered by several limitations. Firstly, although many different critical appraisal tools exist for various types of studies, a validated and specific critical appraisal tool for case series was not identified in the literature. In order to overcome this limitation, three critical appraisal checklists and a guideline for case reports were combined, and a critical appraisal tool was designed, in order to conduct this study. Secondly, as previously stated in this dissertation, many different terms are used to describe lumbosacral disease and the several surgical techniques to treat it. This posed as a limitation throughout the study, particularly when establishing search terms, as part of the search strategy. An attempt was made to overcome this limitation by using a wide range of search terms in the search process. Inability to access some important databases such as: MEDLINE, Embase, BIOSIS Previews, and CAB Abstracts as well as some literature, especially from studies dating previously than 2000; may have prevented the retrieval and appraisal of possibly relevant studies. This was overcome by an extensive search in PubMed, Web of Science, Google Scholar, and hand-search in bibliographic references of review articles and book chapters. The author of the study was familiar with research on the surgical treatment of DLSS, therefore blinding of the screening process was not possible. Furthermore, inclusion and exclusion criteria for studies, as well as criteria for answering the critical appraisal checklist, may have been influenced by previous knowledge of the literature. Because only studies published on peer-reviewed journals and books were included, grey literature was not retrieved, and therefore some studies may have been concealed. Due to exclusion of studies in languages other than Portuguese and English, some important studies in other languages may have equally been missed. The study was conducted by only one author, which makes not only screening, but the totality of the critical appraisal less reliable than if two or more reviewers were to have performed it. Although an attempt was made to establish clear and

objective criteria for answering the questions proposed in the designed critical appraisal tool, its subjective nature poses as a limitation. Several questions included in the tool are directed to the adequacy of the reporting, rather than the risk of bias in the design and conduct of included studies, which has been discouraged (Green et al., 2011). An attempt to overcome this limitation was the inclusion of open-ended questions in the critical appraisal tool. Furthermore, because the quality of reporting influences reader interpretation, its assessment was considered relevant.

V. Conclusions

1. Proposed study characteristics

Although case series are valuable tools to convey important information, stimulate the generation of new hypotheses, and support the emergence of new research (Garg, Lakhan & Dhanasekaran, 2016), they are relatively low in the evidence hierarchy and have limitations such as lack of a control group, tendency to bias (similarly to other observational studies), and often incomplete data collection (especially when they are retrospective in conduct) (Albrecht et al., 2009; Kooistra, Dijkman, Einhorn & Bhandari, 2009). For conditions for which there is no certainty on how to best treat patients, such as DLSS, and in lack of the highest level of hierarchical evidence to provide such information (systematic reviews), randomised controlled trials would greatly benefit current knowledge on the area. In such study design, and in order to limit bias, patients would be random and blindly allocated into the different treatments and then the outcomes assessed by objective measures at specific points and/or subjective measures by blinded assessors (Green et al., 2011; Jeffery, 2014). Several practical limitations are potential obstacles to the conduct of a randomised controlled trial assessing the best treatment option for DLSS. Firstly, each case has specific attributes that limit a random allocation. For example, dorsal laminectomy alone might not be adequate for a patient with clinical signs associated with compression of the L_7-S_1 intervertebral foramen (Jeffery, 2014). Blinding of participants (in this case, owners) and personnel is equally challenging in studies on surgical treatments because veterinarians have an ethical obligation to inform pet owners on what treatment option their animal is going to receive and because medical decisions are based on the results of different diagnostic methods, which would be difficult, if not unethical to conceive.

Reporting guidelines improve the completeness of published scientific reports, so grounding the manuscript of a case series on a validated guideline such as the case report (CARE) guidelines, is advised (Gagnier et al., 2014). A case series on the surgical treatment of DLSS

should begin with a clear title. The words “case series” should appear on it, along with the intervention of greatest interest so that a precocious identification of the topic and goals of a study can be performed by reviewers and veterinary healthcare professionals (Green & Johnson, 2006; Gagnier et al., 2014). Although the decision to include keywords on a paper may depend on specific journal requirements, it has been advised. The use of Medical Subject Headings is preferred (Garg et al., 2016). This is particularly important in studies reporting outcome of treatment for DLSS because lumbosacral disease and its different surgical treatment techniques have been described in the literature through a range of many different terms (Denny et al., 1982; Watt, 1991; Sjöström, 2003; Lanz & Rossmeisl, 2012). Clear clinical inclusion and exclusion criteria should be accurately reported, because they allow case series to be compared against one another. One of the main features that limit criteria for participant selection is the retrospective nature of the literature on the topic. The establishment of prospective studies would overcome this limitation (Da Costa, 2014; Jeffery, 2014). Consecutive inclusion of participants ought to be conducted and clearly reported because it increases case series reliability and credibility, and reduces selection bias (Albrecht et al., 2009; JBI, 2016b). Patient demographic information, such as: age, breed, sex, level of activity, and weight, should be fully reported, so that predisposition and risk factors may be assessed (Sifers et al., 2002; JBI, 2016b). A complete report of the clinical information of all participants in a case series, mainly the findings of physical, neurologic, and orthopaedic examinations, is advised. In addition to prevalence of clinical signs, duration also seems to be an important measure (Jaeschke et al., 1994; Lijmer et al., 1999; De Risio et al., 2001; Linn et al., 2003). Standardisation of diagnostic methodologies increases study reliability, therefore it is recommended (Jaeschke et al., 1994; Lijmer et al., 1999; JBI, 2016b). The diagnostic methodology must rely on existing definitions or diagnostic criteria. Complete history, physical, neurologic and orthopaedic examinations should be performed and fully reported. The maneuver for pain elicitation should equally be described. Advanced diagnostic imaging modalities are becoming increasingly available and are valuable tools to assess *cauda equina* compression, so their use is preferred, when available (Meij & Bergknut, 2010; Dewey, 2013; Jeffery, 2014). Description of which criteria the diagnosis was based on also helps define if the results of a study are reproducible (JBI, 2016b). The complete treatment protocol should be clearly described, so that it can be understood by the reader and replicable (Green & Johnson, 2006; JBI, 2016a). The outcomes and follow-up results also need to be fully reported and measured, especially how outcome measurement was conducted and which type of tools were used by the assessors. Objective outcome measures such as FPA and performance in standardised exercises have been advised (Jeffery, 2014). However,

concurrent use of standardised and validated subjective outcome measures such as owner questionnaires and veterinary lameness scores could also prove to be useful, providing that a caregiver placebo effect is accounted for (Conzemius & Evans, 2012). Blinding of outcome assessment could be used to enrich the conduct of outcome measurement, limiting systematic bias (Jeffery, 2014). Standardisation of outcome measurement would, similarly to standardisation of diagnostic methodologies, increase study reliability, so it is recommended (Schulz et al., 2006). This should include outcome assessment with the same outcome measures and at the same time post-surgically for all participants. Loss of participants to follow-up influences study protocol validity, so it should be limited and clearly reported, if it occurs (Chan & Bhandari, 2011). Because not all reported surgical techniques have assessed long-term postoperative outcome of DLSS treatment, a follow-up of a year or more is recommended based on reports of recurrence of clinical signs in patients which underwent surgical treatment for DLSS (De Risio et al., 2001; Linn et al., 2003). Case series should provide practical clinical guidance for veterinary healthcare professionals, so a summary of key study lessons should also be included (JBI, 2016a).

2. Future prospects

Validation of a critical appraisal tool for case series would greatly benefit and enrich the critical appraisal of such studies. In lack of a validated tool, the one designed for this study may be used for other case series. Although it may be suitable for studies reporting the results of surgical treatment of DLSS, it would require adaptation and modification, especially of the criteria for answering the critical appraisal tool questions, if it were to be used in other types of studies.

Although there are several limitations to the execution of randomised controlled trial or other studies representing higher level of evidence to ascertain which treatment option is the best for patients with DLSS, this study has demonstrated that there is room for improvement of the conduct and reporting quality of case series, so that rigorous data can be generated and analysed, to inform research design, guide clinical practice, and improve veterinary healthcare delivery (Gagnier et al., 2014). However, we must also take into account that even the most robust, prospectively conducted, and clearly reported case series have limitations that make the quality of the evidence they provide incomparable to that provided by well-constructed randomised controlled trials (Kooistra et al., 2009).

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Annexes

Annex 1 – Search terms

PubMed:

(dog OR dogs OR canine OR canidae) AND (surgical treatment OR dorsal laminectomy OR dorsal decompression OR decompression OR decompressive OR distraction fusion OR Fixation Fusion OR fixation OR Fusion OR stabilization OR Foraminotomy OR Lateral Foraminotomy) AND (Degenerative lumbosacral stenosis OR lumbosacral disease OR cauda equina syndrome OR lumbosacral stenosis OR cauda equina compression)

Web of Science: (1900-present)

(dog OR dogs OR canine OR canidae) AND (surgical treatment OR dorsal laminectomy OR dorsal decompression OR decompression OR decompressive OR distraction fusion OR Fixation Fusion OR fixation OR Fusion OR stabilization OR Foraminotomy OR Lateral Foraminotomy) AND (Degenerative lumbosacral stenosis OR lumbosacral disease OR cauda equina syndrome OR lumbosacral stenosis OR cauda equina compression)

Google Scholar (1900-present)

(cão OR cães OR canídeo OR canidae) AND (síndrome de cauda equina OR doença lombossagrada OR doença lombosagrada OR estenose lombossacral OR estenose lombossagrada) AND (laminectomia OR laminectomia dorsal OR foraminotomia OR fusão OR fixação)

Annex 2 - Critical appraisal tool for case series assessing the results of surgical treatment for degenerative lumbosacral stenosis in the dog

1 - Were there criteria for inclusion and exclusion in the case series?

YES__ NO__ Unclear__ Not applicable__

Which criteria were used?

_____

2 - Did the case series have consecutive inclusion of participants?

YES__ NO__ Unclear__ Not applicable__

3 - Was there clear reporting of the demographics of the participants in the study?

YES__ NO__ Unclear__ Not applicable__

4 - Was there clear reporting of clinical information of the participants?

YES__ NO__ Unclear__ Not applicable__

5 - Was the condition measured in a standard and reliable way for all participants included in the case series?

YES__ NO__ Unclear__ Not applicable__

6 - Were valid methods used for identification of the condition for all participants included in the case series?

YES__ NO__ Unclear__ Not applicable__

Which methods were used?

_____

7 – Was the intervention or treatment procedure clearly described?

YES__ NO__ Unclear__ Not applicable__

8 – Were the outcomes or follow-up results of cases clearly reported?

YES__ NO__ Unclear__ Not applicable__

How were outcomes reported and measured?

_____

9 – Does the case series provide takeaway lessons?

YES__ NO__ Unclear__ Not applicable__

10 – What was the follow-up rate of the study?

_____