



Regulatory Mechanisms in Biosystems

ISSN 2519-8521 (Print)
ISSN 2520-2588 (Online)
Regul. Mech. Biosyst.,
2023, 14(3), 386–392
doi: 10.15421/022357

Densitometric correlates of degenerative-dystrophic processes in cervical vertebrae of humans and domestic animals

T. O. Andreyeva*, O. M. Stoyanov**, G. M. Chebotaryova***,
V. I. Kalashnikov****, R. S. Vastyanov**, S. S. Mashchenko*****

*Petro Mohyla Black Sea National University, Mykolaiv, Ukraine

**Odesa National Medical University, Odesa, Ukraine

***Odesa Polytechnique University, Odesa, Ukraine

****Kharkiv National Medical University, Kharkiv, Ukraine

*****Ukrainian Research Institute of Transport Medicine, Odesa, Ukraine

Article info

Received 23.06.2023

Received in revised form 21.07.2023

Accepted 02.08.2023

Petro Mohyla Black Sea National
University, Desantnykiv st., 68,
Mykolaiv, 54000, Ukraine.
Tel.: +38-063-838-98-89.
E-mail:
tamara.andreyeva@gmail.com

Odesa National Medical University,
Valihovskiy Lane, 2, Odesa, 65082,
Ukraine. Tel.: +38-048-723-42-49.
E-mail: anstoyanov@ukr.net

Odesa Polytechnique University,
Shevchenko Avenue, 1, Odesa, 65044,
Ukraine. Tel.: +38-067-752-10-03.
E-mail:
a.m.chebotareva@gmail.com

Kharkiv National Medical University,
Nauki av., 4, Kharkiv, 61000, Ukraine.
Tel.: +38-057-707-73-80.
E-mail: dr.valkalash@gmail.com

Ukrainian Research Institute
of Transport Medicine, Kanatna st., 92,
Odesa, 65000, Ukraine.
Tel.: +38-094-950-25-03.
E-mail:
dr.mashenkos@gmail.com

Andreyeva, T. O., Stoyanov, O. M., Chebotaryova, G. M., Kalashnikov, V. I., Vastyanov, R. S., & Mashchenko, S. S. (2023). Densitometric correlates of degenerative-dystrophic processes in cervical vertebrae of humans and domestic animals. Regulatory Mechanisms in Biosystems, 14(3), 386–392. doi:10.15421/022357

The cervical spine is the most mobile region with high work activity which constantly receives a heavy load. This region is the least protected from external influences, especially in cases of degenerative-dystrophic changes. A comparative analysis of clinical-morphological and morphometric data in degenerative-dystrophic lesions of the cervical spine in humans and domestic animals with secondary anatomical and physiological abnormalities was performed. The examined contingent of people was of young and middle age (average age equal to 41.5 ± 5.2 years). The examined animals had a similar age range recalculated to human age. The pathological changes in spinal cord configuration were registered in 84.6% of examined humans ($n = 65$) in the form of angular kyphosis or straightened lordosis (with the analogous relative distribution). In terms of gender, with the exception of the frequency of angular kyphosis, probable differences in the formation of lordosis, which is straightened (2.1 times more often), the indicators were the same while the normal configuration of the spine was more often registered in men against the women (20.0% vs 12.5%). Cervical spine deformations in different breeds of dogs and cats ($n = 75$) were observed in 34.7% of cases (angular kyphosis – 38.5%; straightened lordosis – 61.5%). Preservation of normal configuration of the cervical spine was recorded more often in cats – 78.6%, and in small breeds of dogs – 78.5%. In large breeds of dogs, these indicators were probably changed: the norm remained only in 26.3%, and the deformations exceeded the corresponding indicators in cats and small breeds of dogs by 2.7 or more times. The significant differences were found in cases of straightened lordosis formation which was registered more often in women than in men. The incidence of angular kyphosis was comparable in patients of both sexes. Cervical spine deformations in different breeds of dogs and cats were observed in 26 animals (34.6% cases: angular kyphosis – 13.3%; straightened lordosis – 21.3%). The density of vertebral bodies in all groups decreased in the caudal direction of the cervical spine. The differences in humans reached 18.1%, being higher in women than in men. Animals had a similar density distribution. This index was minimal in cats (2.7%), in small-breed dogs it increased significantly (7.5%) and in large-breed dogs it reached 14.3%, i.e. 5 times (compared to cats) and 2 times higher (compared to small breed dogs). A comparative analysis between humans and animals indicates that the maximal discrepancies in the studied indexes were found in humans and relatively coincided with those in large breed dogs. The presence of neurological deficit with cervical spine pain syndrome with lordosis distortion and the provocation of spinal canal stenosis was found in 73.7% of large adult dogs. The revealed regularities of cervical spine degenerative-dystrophic changes indicate that animals, especially large breeds of dogs, can serve as a model for investigation of etiopathogenetic factors, clinical course, prognosis and other risks of the bone-cartilage apparatus degeneration with both stenosis and vertebrogenic myelopathy development at the cervical level in humans. The obtained clinical and morphometric data from comparative analysis in humans and domestic animals will serve as the basis of methods of prevention of degeneration in the bone-cartilage apparatus and the premature aging of the body in humans.

Keywords: vertebrae; human cervical spine; dogs; cats; changes in the spine configuration; density of the vertebrae; degenerative-dystrophic processes; osteochondrosis.

Introduction

The cervical spine is the most complex joint system in the human body which contains thirty-seven separate joints that provide multiple head and neck movements in relation to the body and, in addition to the motor-extrapyramidal system, are subject to all specialized sense organs. The seven cervical vertebrae with their capsular, ligamentous, tendinous, and muscular attachments do not protect their contacts compared to the

skull and thorax (Kaiser et al., 2021). The contents of this anatomical cylinder, located between the skull and the chest, include the carotid and vertebral arteries, the spinal cord and all frontal and back nerve roots as well as the brainstem (Bland & Boushey, 1990).

Degenerative-dystrophic lesions of the cervical spine significantly affect the quality of life of both humans and animals causing the development of neurological deficits, movement restrictions and pain syndrome. The latter is a growing problem, in ten years its frequency (with pain las-

ting more than 3 months) has increased by 21% and can reach 41% (Saini & Mukhdomi, 2022). The prevalence of spinal canal stenosis in the presence of clinical symptoms is well known to have reached 80%, with an asymptomatic course – from 14% to 24% (Smith et al., 2020). Diseases of the muscle-skeletal system and connective tissue rank third place among the adult population of Ukraine with a steady upward trend. In Ukraine, up to 350,000 cases of primary osteoarthritis are registered annually, of which more than 60% are in people of working age (Afanasyev & Maikova, 2017). According (Rupp, 2020), 266 million people (3.6%) worldwide suffer from spinal cord diseases annually: the maximal in Europe (5.7%) and the minimal in Africa (2.4%). Annually, 39 million people (0.5%) worldwide suffer from spondylolisthesis, 403 million (5.5%) people have symptomatic disc degeneration and 103 million (1.4%) people worldwide suffer from spinal canal stenosis (Ravindra et al., 2018). The frequency of the spine osteochondrosis affecting people of the most active social group is from 20% to 80% of temporary disability cases (Bohndorf, 1998). The pain syndrome dominates in the neck and back regions in cases of degenerative-dystrophic clinical picture of the cervical spine, which affects more than half of the world's population, and whose prevalence in industrialized countries is 60–80% (Yemecz et al., 2020). Research on chronic pain and neurological symptoms has determined that C₅–C₇ level is one of the important cervical spine levels which normally forms a physiological lordosis in humans and animals.

Cervical lordosis is important for many processes including chewing, respiration, vocalization, eye and gaze movements, as well as spine cushioning during walking and running (Been et al., 2017). The cervical spine distortion has important clinical sequences (Nightingale et al., 1996; Kawakami et al., 1999). The achievement of moderate cervical lordotic curvature has been found to be associated with better surgical outcomes in patients with neurological deficits (Baba et al., 1996; Stein, 1997; Swank et al., 1997). The restoration of cervical lordosis after surgery is also considered to be important as otherwise the neural tissue compression can lead to its damage (Harrison et al., 2002).

The scientists of the American Geriatric Society studying chronic pain in elderly patients pay great attention to algic syndromes and methods of treatment of their accompanying neurological symptoms, which requires further clarification and study. The motor and reflexory manifestations are noted, respectively, in the involved segment between C₅ and C₆: the lower limbs, fingers and forearms paralysis, shoulder abduction and elbow flexion weakness as well as loss of reflex from the biceps muscle of the shoulder; the analogous disturbances at the level between C₆ and C₇ provoke movement disorders in the legs and distal parts of the hands with preserved mobility in the shoulder and elbow joints (Gloth et al., 2001). Spine pathophysiological and organic changes (marginal osteophytes of the vertebral bodies, degenerative and inflammatory processes in the intervertebral joints, hypertrophic manifestations in the dorsal longitudinal and yellow ligaments, the spinal canal congenital and acquired stenosis) objectively revealed on a CT scan can explain the pain syndrome occurrence and strengthening of its expression due to compression of the blood vessels, ischemic manifestations and edema of the adjacent tissues. These circumstances became the reason for referral of our patients to a cervical spine CT examination. It's important that cervical spine degenerative-dystrophic changes, including stenotic, during neuroimaging do not always correlate with clinical symptoms and signs of myelopathy (Nurmieva & Bogdanov, 2011).

In all cases, when evaluating the X-ray densitometric characteristics of the bone structures of the vertebral-motor segments in patients with intervertebral osteochondrosis, there is a discrepancy between the data on the density of bone tissue in the central parts of the vertebral bodies and brackets, which also indicates the patterns that exist between the biomechanics and morphology of bone tissue as a result of the repeated exposure to functional load (Hussein et al., 2013). It is known that bone trabeculae are remodeled according to trajectories of load exposure with changes in bone tissue with the presence of osteoporosis and osteosclerosis areas, which indicates the “remodeling bone power”. The bone changes its internal architecture with the help of trabeculae intratissue growth and direct reconstruction, and mechanical factors have a crucial influence on the formation of external shape of the bone, causing its deformation (Mann & Ralston, 2003; Anderst et al., 2011).

Pathological changes in the cervical spine – cervical scoliosis, osteochondrosis, etc. – are a significant cause of a number of diseases associated with disorders of the blood supply to the brain. Such changes in the spinal structures develop under the influence of various factors, an important place among which is hypodynamia, inadequate physical activity, as well as constitutional and anthropometric features of the body structure. Early diagnosis of this kind of changes under the influence of adverse factors is possible only under the condition of deep and perfect knowledge of age, gender, constitutional and individual features of the morphology of the studied area (Adamovych, 2016).

The Quantitative Computed Tomography allows us to analyse the cancellous and cortical bone tissue, their mineral density. Macro- (bone geometry) and microstructural (size and number of bone trabeculae) components are also evaluated (Riggs & Melton, 1995; Adams, 2009).

It is known that, according to the stages of lordosis classification, during the degenerative-dystrophic process of the cervical spine changes in physiological lordosis occur, which contribute to pathomorphological deformations of the entire spine, spondyloarthritis, osteophytes and spondylolisthesis development, the congruence of the intervertebral joints facets is disturbed, deformations of the vertebral bodies in the form of platyspondylia, bradyspondylia, narrowing of the intervertebral holes, subchondral sclerosis and, as a result, stenotic changes in the spinal canal and intervertebral holes (Mikhailov & Abelskaya, 2015).

It is important that not enough attention is paid to the study of the processes of pathological deformation, the density of the spinal cord vertebrae with the help of clinical and morphometric analysis in animals. In fact they are not even diagnosed, or they are detected in the late stages of the disease with the listed clinical picture and require urgent, not always effective surgical intervention.

The aim of the study was to determine the efficacy of early diagnostic procedures for evaluation of degenerative-dystrophic processes in the cervical spine using clinical and morphological investigation of spine vertebral bodies in humans and animals.

Materials and methods

In our studies, all the manipulations with animals were verified by the local bioethical committee of the A. V. Palladin Institute of Biochemistry of the NAS of Ukraine for the conformity to the recommendations of the European Convention for the Protection of Vertebrate Animals used for Research and Scientific Purposes (Strasbourg, 1986) and the Law of Ukraine “On Protection of Animals from Cruelty” and are ethically acceptable. This study included data from a medical examination of persons who gave written agreement. All laboratory veterinary studies were performed absolutely with the permission of the dog owners. The complex clinical and laboratory studies performed were painless, non-invasive and took into account the individual condition of each patient and dog. Violations of the norms of bioethics were not observed.

Clinical and morphometric studies were performed together with comparative CT studies of cervical spine degenerative-dystrophic processes in humans and animals accompanied by pain symptoms of varying intensity and frequency with neurological deficits. Cervical spine CT-investigation data of 65 patients were analyzed retrospectively with the aim of comparative description of the radiological picture vertebral bodies, investigation of morphometric densitometric changes and physiological lordosis distortion. Our research examined 25 men (38.5%) and 40 women (61.5%) aged from 20 to 65 years (average age equal to 41.5 ± 5.4 years).

Clinical and morphometric studies together with and CT studies were conducted on 75 animals: 14 cats, 42 dogs weighing up to 20 kg and 19 large breed dogs above 20 kg with clinical manifestations of motor disorders, acquired behaviour and neurological symptoms in response to nociceptive reactions in the neck and back regions. Randomization of the animals by age coincided with the average age of humans. The age of dogs was converted to human age (Tjahjadi & Onibala, 2010; Patel et al., 2020; Teo, 2020; Yates, 2021) using the developed formula: human age = 16 x (dogs age natural logarithm) + 31. The calculation of the formula is based on the quantitative aging transfer from dogs to humans by conservative remodelling of epigenetic networks (Wang, 2020; Yates, 2021). Thus,

the average age of dogs transferred into human age was 43.4 ± 7.0 years, which was identical to the average age of the studied humans – 41.5 ± 5.2 years.

We used the following criteria for inclusion of patients into the study: pain syndrome in the upper part of the trunk, disorders of segmental innervation, mainly in the upper extremities and the presence of cervical spine degenerative-dystrophic processes. Similar clinical disorders in animals also served as criteria for their inclusion in the study.

The following criteria were used to exclude patients from the study – the presence of degenerative-dystrophic processes with comorbid pathology: developmental anomalies, dysplasia and dysraphia of the vertebral bodies and intervertebral joints, osteoporotic and cystic changes in the vertebral bodies, oncopathology, diagnosed osteoporosis and systemic connective tissue diseases. Animals were excluded from the study in the presence of pathological processes similar to those in humans. Chondrodystrophic dog breeds were also excluded from the study.

The pain syndrome intensity in humans was recorded using a 10-point visual analogue scale (VAS) graduated from 0 to 10 (Stoyanov et al., 2015). This is the most convenient for the patient due to ease of use and for the researcher due to fast statistical processing.

Clarifying terms were added along the ruler for maximum assistance in assessing pain: near each point one could see “weak”, “moderate” and “severe”. The distance between the end of the line (“no pain”) and the mark made by the patient was measured in cm and rounded off. The patient indicates the place on the digital canvas of the ruler, which, in his opinion, corresponds to the intensity of pain. The following ranks of the pain sensation was used: weak pain corresponds to 1–4 section of the ruler, moderate pain – 5–6 and severe – 7–10 points (Kharchenko, 2014).

The intensity of pain in animals was recorded using a five-point visual analogue scale (from 0 to 4 points) (Hielm-Björkman et al., 2011) paying attention to habitus, gait, behaviour, response to palpation and body tension (Mathews et al., 2014; Hernandez-Avalos et al., 2019). This scale is actively used in veterinary medicine. Pain intensity was assessed in the range from 0 to 4 units, i.e. 0 means no pain, and 4 means maximal pain (Hielm-Björkman et al., 2011).

Examination of individuals was performed at LLC "Medkoryug," License No. 565755, series AV, using the Somatom Definition AS CT scanner (2017) by Siemens (Munich, Germany), in Dicom mode, with WorkStream 4D™ for optimal workflow organization and CARE Dose 4D for radiation dose optimization, along with the standard image processing program Syngo Osteo. For animal examinations, the MX 8000 CT scanner by Philips (Amsterdam, Netherlands, 2002) was used, based at LLC "Veterinary Center "Favorit," License No. 571, issued on July 19, 2017, in Dicom mode. For optimal visualization of the cervical spine in humans and animals, post-processing was performed to construct multiplanar 3D reconstructions using Horos Viewer software for animals and WorkStream 4D™ for human image processing. The use of additional software options, such as multiplanar reconstructions, MIP, and MIP thin VRT (multiplanar reconstructions), improved diagnosis. Measurement of morphometric and densitometric body density was conducted in Hounsfield Units at the location of maximum impact of intervertebral osteochondrosis, which corresponds to the peak of physiological lordosis, specifically at the C₅–C₇ level.

Multislice and multiplanar tomography scanners with a collimation of 1.0–1.5 mm were used to achieve high resolution during spine examinations. This allows for the creation of an almost isotropic data array, ensuring high-quality multiplanar reconstruction in any direction. When selecting the pitch factor (P) of 0.75–0.90, step artifacts are less pronounced in scans with thin slices. Thin slices reduce the partial volume effect and, consequently, also decrease streak artifacts caused by increased rigidity. Standard scanning protocol parameters for both humans and animals include the following indicators: field of view in millimeters, scan length in millimeters, view angle in degrees, voltage (kV), current (mA), and the scanning or reconstruction filter mode (C-soft tissue mode, D-bone mode). Scanning parameters differ between humans and animals based on anatomical principles, the volume of the scanning area, the length of the examination region, and the thickness of neck structures.

The morphometric-densitometric measurement of density of the vertebral body's was carried out in Hounsfield units, in the localization of the

maximal impact at the top of the physiological lordosis, i.e. C₅–C₇ level. Scanning protocols for humans and animals took into account the generally accepted recommendations of the computed tomography manufacturer and were standard. During CT examination, patients were placed on their backs, arms along the body, maximally expanded dorsally to avoid artifacts when scanning the cervical spine from the denser bones of the shoulder girdle.

The animals' position during CT examination was standard: in sedation with muscle relaxation, on the stomach, the legs in the physiological position were extended frontally – to front, from back side – along the body. For very large dogs (weighing over 20 kg) a side position is possible, with a pad between the front and back of the limb. In any case, the limbs should be at the same level to achieve maximal symmetry.

The cervical spine scanning in humans is performed at the depth of inhalation with breath holding; in animals, the entire scanning area was covered, which was achieved by general anesthesia with muscle relaxation. To obtain the most accurate data during CT examinations, patients were positioned so that the exact location of the region of interest was in the center of the gantry aperture (which is achieved using a laser in two planes) by reducing X-ray cone beam artifacts. All human images were obtained with patients' lying on their back relative to the CT scan table with maximal inspiration; animals were located either prone or laterally in a position convenient for scanning, in conditions of sedation and muscle relaxation.

The following parameters were the subjects of the study – the comparative characteristics of human cervical spine tomography, analysis of the vertebrates' body – the sagittal size (Sag), the morphometric data related to the spinal canal – diameter at the C₆ level (SagD). The Pavlov-Torg index was used when the size of the human spinal canal was less than 12 measurement – in this case it was usually equal to 1 (Tjahjadi & Onibala, 2010; Morales-Avalos et al., 2018). The reserve space was calculated by subtracting the spinal cord sagittal diameter from the spinal canal sagittal size. The relative normal value for a certain patient is the C₃ vertebral body Sag morphometric data measurement and the spinal canal width at this level which is the widest part. This level, according to statistics, is the least prone to degenerative-dystrophic process manifestations. The C₆–C₇ level – the peak of physiological lordosis – in humans and animals is the narrowest anatomically, in which lesions are most often recorded.

All veterinary studies are performed with the permission of the animals' owners. Instrumental studies and clinical manipulations were painless, non-invasive, taking into account the individual condition of each patient and animal. All studies were performed in accordance with existing bioethical standards.

The data obtained were presented as mean (\bar{x}) and the standard error of the mean (SE). One-way analysis of variance (ANOVA) followed by Newman-Keuls post-hoc test was used to detect the significant differences between the investigated groups. The Nonparametric Kruskal-Wallis test was used to detect significant differences. In the case of using raw absolute indexes $P < 0.05$ was considered as statistically significant difference.

Results

The pain syndrome was the leading clinical factor and was revealed in all examined patients. It was predominantly complex in the form of cervical pain accompanied with pain in the upper part of the spine with typical radiation to the upper limbs. The intensity of pain according to VAS in some cases reached 5 points.

Regional disorders of segmental innervation and pyramidal manifestations were revealed. Mild paresis of the upper limbs were observed (48 patients) localized mainly in the distal parts of the upper limbs. There were complaints about weakness in the hands (48 patients): in one hand (14 patients), in both hands (34 patients); weakness in the legs – in 13 patients, gait changes – in 12 patients; fascicular twitches – in 2 patients; the intensified tendon reflexes in the legs – in 32 patients. Numbness in the upper limbs was registered in 30 patients, other sensory disorders were identified in 24 patients; myalgia – in 15 patients; muscle atrophy – in 14 patients; pelvic reservoir disorders – in 7 patients who had the expressed greatest manifestations of cervical spine stenotic changes.

According to CT scan, degenerative-dystrophic processes in the spinal cord bodies were diagnosed in the form of deforming spondyloarthrosis

manifestations in 51 patients, narrowing of the intervertebral openings – in 47 patients, deforming spondylolisthesis – in 30 patients, the longitudinal and yellow ligament connection hypertrophy – in 42 patients. The pathology listed above determined the degree of spinal curvature, the clinical picture of compression myelopathy, stenotic changes as well as persistent pain syndrome.

We evaluated the animals' behaviour, their pain reactions, and the owners' complaints about pain manifestations were analyzed. Visually and during the objective examination, changes in habit, gait, of various kinds, limping, depressed behaviour, painful reaction to palpation, unusual local tension of the body were revealed. It should be noted that the above listed symptoms were often combined with each other.

Signs of the spinal cord damage were observed in majority of the adult dogs (6–14 years old) of large breeds, in the presence of stenosis – in 15 examined animals. Slight weakness of one – 12 animals or both frontal limbs – 3 animals, one and both hind-limbs was detected in 4 animals. Sometimes one could hear the “claws rustling” on the asphalt in 10 animals.

Neurological symptoms in the form of atypical paw position, limb muscles tone decrease/increase (or dystonia) were considered as the pyramidal insufficiency manifestations. They were diagnosed more often in large and giant breeds, to a lesser extent in dogs weighing less than 20 kg, and only rare manifestations have been noted in cats. The stato-dynamic peculiarities analysis in dogs show that discomfort when getting up from a “sitting” or “lying” position is registered in 9 small and 10 large dogs; statolocomotor changes – in 7 small and 8 large dogs; pelvic reservoirs disorders – in 2 small and 3 large dogs. A local pain syndrome during cervical spine palpation was detected in 15 large animals, and it was associated with stenotic changes, root and ischemic syndromes, nerve conductors and corresponding involvement of reflectory zones and tonic tension of the neck muscles. Objective examination of large animals revealed that clinical symptoms were 2–3 times more expressed ($P < 0.05$) compared with the same symptoms presence in dogs of medium and small breeds in the presence of cervical spine degenerative-dystrophic changes.

We found the physiological lordosis was preserved in 15.4% of all patients. It prevailed in men (20.0%), in women this indicator was lower by 7.5% ($P < 0.05$). The pathological deviations of spine configuration (lordosis rectification – 43.1% and angular kyphosis – 41.5%) were equal to 84.6% ($P < 0.05$). Straightened lordosis prevailed in women (by 11.5%), and angular kyphosis had no gender differences and was almost equally common in men (44.0%) and women (40.0%; Table 1).

Table 1

Changes in the spine configuration of the examined patients and domestic animals

Groups of investigations	Cervical spine lordosis forms (absolute indexes)		
	control	angular kyphosis	straightened lordosis
Patients			
Male, n = 25	5*	11	9*
Female, n = 40	5	16	19
Domestic animals			
Cats, n = 14	11 ^c	1 ^b	2 ^b
Dogs weighing less 20 kg, n = 42	33 ^c	4 ^b	6 ^b
Dogs weighing above 20 kg, n = 19	5 ^{ab}	5 ^{ab}	9 ^a

Notes: * – $P < 0.05$ – significant differences in the indexes compared with the same in female patients (Kruskal-Wallis test); ^a – $P < 0.05$ significant differences in the investigated indexes compared with those in dogs weighing less 20 kg (Kruskal-Wallis test); ^b – $P < 0.05$ and ^c – $P < 0.01$ – significant differences in the investigated indexes compared with those in examined patients (one-way ANOVA test followed by Newman-Keuls post-hoc test).

In multiplanar post-processing CT scans 3D reconstructions of domestic animals physiological lordosis distortion was detected, mainly in dogs of large breeds compared with the corresponding clinical symptoms in cases of cervical spine degenerative-dystrophic changes (Table 1). CT data were correlated with the clinical and diagnostic picture. Analogous indexes in animals statistically more often referred to normal forms of cervical spine lordosis. We registered the physiological form of lordosis prevalence in cats and dogs weighing less than 20 kg (78.6% and 78.5%, respectively; $P < 0.05$). This index in large breeds dogs was equal to 26.3%, was lower in small breeds of dogs ($P < 0.05$) and was close to the analogous values obtained in humans (being higher in 1.7 times).

Physiological lordosis distortion was detected in 3 cats (21.4%) of the oldest age (11–14 years) with minimal clinical data for this species of animals. Similar indexes were registered in small breeds of dogs with a prevalence of older age groups.

We registered the most expressed spine configuration changes in large breed dogs in which the lordosis modifications reached 73.7%, i.e. they were 3 times higher compared with the same index in other groups ($P < 0.05$). Relative changes in the spine approached those of humans only in the group of large breed dogs (Table 2).

Table 2

The average densitometric data of the vertebral bodies density in patients

Examined patients	C ₃ vertebra body density	Cranial vertebra body density	Caudal vertebra body density
Male, n = 25	417 ± 33	451 ± 63	348 ± 48
Female, n = 40	433 ± 29	510 ± 52	440 ± 45

Notes: there are no significant differences of investigated indexes (one-way ANOVA test followed by Newman-Keuls post-hoc test).

With degenerative changes shown on cervical spine CT scans and in cases of clinical examination of segmental neurological deficit and pain syndrome manifestation it was determined that the C₆ level had the greatest deformation in conditions of cervical lordosis in humans and animals despite the different posture of the examined groups.

The CS bodies morphometric-densometric density was determined in Hounsfield units. We accepted these data at the C₃ level as a relative norm for patients since there were no changes in the body of the vertebra and the intervertebral disc at the C₃ level.

While comparing the C₃ vertebra body density with the cranial and caudal vertebrae density at the level of lesion (in most cases in humans this is the C₆ body and the C₅–C₇ bodies level) we obtained a pattern in which the cranial vertebrae density increases while the distal vertebrae density decreases, which is probably due to the characteristic application of force and mechanical energy (Table 3).

Table 3

The average densitometric data of the vertebral bodies density in domestic animals

Animals, n = 75	C ₃ vertebra body density	Cranial vertebra body density	Caudal vertebra body density
Cats	524 ± 80	525 ± 71	511 ± 76
Dogs weighing less 20 kg	543 ± 47	491 ± 50	454 ± 41
Dogs weighing above 20 kg	570 ± 53	471 ± 47	404 ± 51

Notes: see Table 2.

We determined the ratio between the vertebra density, the lordosis curvature and dynamic load after the data obtained using the CT technique with analysis and comparison of X-ray CT scans. The vertebrae densitometric density as well as cranial and caudal vertebrae densities in women were found to be higher in C₃ level compared to similar indexes in men.

Although the way of life of animals differs from that of humans and despite the anatomical and physiological differences between them, both humans and animals have similar pathophysiological processes which should be transferred according to age restrictions. Therefore, we noted that the pain syndrome is affected by degenerative changes in the cervical spine. All these factors interact with each other, affect structural, ischemic, clinical and other manifestations, i.e. accelerate aging.

The investigation of the average densitometric data of the C₃ vertebra body density (which is accepted to be normal value) and cranial and caudal vertebrae density was important for determining the influence of degenerative-dystrophic processes in the vertebrae of different species of animals for animals selection as a clinical models (Table 3).

It was shown with the help of the prospectively performed CT scans in the sagittal plane multiplanar 3D reconstructions and post-processing that the peak of physiological lordosis is the C₆ level in all small animals. It was determined that the degenerative-dystrophic process and the physiological lordosis distortion were most visualized and clinically expressed only in large and giant breeds of dogs weighing above 20 kg. Rare cases of cervical spine distortion were detected in small dogs and in a much smaller number in cats. The degenerative-dystrophic process of the neck is one of the reasons for change in the physiological lordosis of the cervical

spine. Organic, pathophysiological, and pathomorphological changes in the cervical spine can provoke back pain, neurological symptoms and worsen people's quality of life.

Objective neurological examination of large animals showed that clinical symptoms were in 2–3 times more expressed ($P < 0.05$) compared to dogs of medium and small breeds in the presence of degenerative-dystrophic changes.

If we consider that the degenerative-dystrophic process in the cervical spine can serve as a predictor for premature ageing in young and middle-aged people, then the study of new etiopathogenetic mechanisms and the use of dogs of large and giant breeds may become highly relevant, taking into account the fact that physiological processes in dogs occur radically faster. With such modeling, the results of new schemes and methods of treating people could be highly promising and useful for investigation of both etiology and pathophysiological mechanisms of pain syndrome. Successful pharmacological treatment performed with pathophysiological background in these conditions will improve the quality of people's lives.

Discussion

Therefore, we performed a significant experimental, laboratory and clinical set of trials to manage the problem of how to diagnose adequately stenosis of the cervical spine. Stenosis of the cervical spine, narrowing of the spinal canal and/or the neck spinal nerve canals, spinal cord or nerves did provoked pain, numbness, tingling and weakness in the neck, shoulders and limbs, neurological manifestations of cervical myelopathy (Joshua & Ammerman, 2019).

Marginal bony growths of the vertebral bodies and the articular surfaces of the intervertebral joints, deformation of the vertebral bodies in the form of bradyostyolysis or platostyolysis, straightened cervical lordosis or the angular kyphosis formation, changes in the densitometric density of vertebral bodies, and therefore metabolic processes in bone structures, endplates and intervertebral discs are known to induce irreversible pathological and organic changes in the nervous system with accompanying clinical symptoms (Ezra et al., 2020). That is why we attracted attention to the vertebrae deformation and the spinal canal narrowing in conditions of changes in physiological lordosis.

Thus, it was shown that pathological changes in cervical spine configuration as the result of degenerative-dystrophic lesions in the examined patients reached 84.6% in the form of angular kyphosis or straightened lordosis (with the same relative distribution). In terms of gender, with the exception of the frequency of angular kyphosis (44.0% and 40.0%), there were probable differences in the formation of lordosis, which is straightened (2.1 times more often). At the same time, the normal configuration of the spine was registered more often in men against women.

Deformations of the spine in the cervical region in the examined different breeds of dogs and cats were observed in 34.6% of cases (angular kyphosis – 13.3%; straightened lordosis – 21.3%). Preservation of the normal configuration of the SCV was significantly more frequent: in cats – 78.6%, in small breeds of dogs – 78.5%. However, in large breeds of dogs, these indicators were probably changed: the norm remained only in 26.3%, and deformations exceeded the indicators of cats and small breeds of dogs by 2.7 or more times.

McAviney et al. (2005) found a significant association between cervical spine pain and lordosis $< 20^\circ$ and a “clinically normal” range for cervical lordosis of $31\text{--}40^\circ$. It was suggested that maintaining lordosis in the range of $31\text{--}40^\circ$ can be a clinical goal of manual therapy treatment.

Pathological changes in cervical spine configuration due to degenerative-dystrophic lesions in the examined contingent of people reached 84.6% and were characterized by clinical manifestation of angular kyphosis or straightened lordosis (with the same relative distribution). We followed certain gender differences in the formation of straightened lordosis, which was registered 2.1 times more often in female than in male patients while normal spine configuration prevailed in men compared with women. The frequency of angular kyphosis was similar in the male and female contingents of patients.

Cervical spine deformations in the different examined domestic animals were observed in 34.7% of cases (angular kyphosis – 38.5%; straightened lordosis – 61.5%). Preservation of normal cervical spine configura-

tion was registered frequently in 78.6% of cats and in 78.5% of small breeds of dogs. The investigated indexes in large breeds of dogs, however, were significantly changed: the normal profile remained only in 26.3% of animals and deformations exceeded the same indexes in cats and small breed dogs by 2.7 times.

A comparative analysis of the cervical spine deformation in all examined groups indicates that, despite the similar anatomical structure of the studied spine, the crucial features of its axial load, posture, statolocomotors, and gaits with the greatest similarity to humans were found only in large breeds of dogs in which all the investigated indexes of spine deformation resembled the same in humans. Such dog breeds we suppose could be a model for investigation of pathological etiopathogenetic factors of cervical spine bone-cartilage apparatus together with neurological complications and pain syndrome as well as providing adequate possibilities for prevention and treatment of degenerative spinal injuries.

Measurements were made regarding the C_3 vertebra body density in patients with cervical spine degenerative-dystrophic processes while there were no changes in the body of the vertebra and the intervertebral disc. These circumstances made it possible to conduct comparative measurements between the above-mentioned level and the most affected and deformed vertebrae $C_5\text{--}C_7$ (C_6) which were the pathological lordosis apex.

The obtained data determined the dependence of vertebral density on the level of curved lordosis and dynamic load.

Analogous morphometric measurements were taken in all groups of animals. The animals' morphometric data was shown to coincide with the same measurements in human observations in conditions of degenerative-dystrophic processes and pathologically curved lordosis. However, such changes were mostly visualized in the following row of examined animals: large breed dogs – small breed dogs – cats (rare cases, and mostly at an older age).

The density of the vertebral bodies in all groups was shown to be decreased in the caudal direction of the vertebral column. In humans, this indicator was the most expressed and the differences reached 18.1%. We found that the vertebrae density in women was compared to men.

Animals had a similar density distribution. However, in cats this indicator was minimal (2.7%), in small breed dogs it increased significantly (7.5%), and in large breed dogs it reached 14.3%, i.e. 5 times higher (compared to cats) and 2 times higher (compared to small breed dogs).

A comparative analysis between humans and animals indicates that the maximal differences were in humans and relatively coincided only with large-breed dogs.

Despite the information regarding degenerative-dystrophic changes in the spine mainly in older age people, such cervical spine manifestations were also observed in patients of younger and middle age. Such a tendency in a similar age range was registered only in large breed dogs, i.e. one could see a clear disease “rejuvenation” in both humans and some animals, which requires further study of this pathology.

Such type of changes in small breeds of dogs and cats was registered mainly at an older age (11–14 years), which we consider to be an aging predictor of spinal structures and the whole body.

The age category of the examined patients refers to young and middle age. At the same time, the examined animals had a similar age range in terms of human age as well as cervical spine bone-dystrophic changes.

The signs of spinal cord spondylogenic compression with neurological deficit at the cervical level in the presence of lordosis curvature and spinal canal stenosis provocation were found in 73.7% of large adult dogs. Thus, the revealed regularities of clinical and morphometric analysis of degenerative-dystrophic changes in the cervical spine indicate that animals, especially dogs of large breeds, can serve a model for investigation of degeneration of the bone-cartilage apparatus and vertebrogenic myelopathy at the cervical level, etiopathogenetic factors, clinical manifestation, prognosis and other risks in humans.

Further clinical and morphometric studies and comparative analysis of the obtained data on humans and animals with pathological deformations of the cervical spine, especially in large-breed dogs, will allow us to predict the course and progression of its damage, because physiological and pathophysiological processes in animals are much faster than in humans. To increase the reliability of research, we consider it important to take into account that the degree of expression of the pathological process,

clinical and morphometric data on cervical spine pathology of animals depend on their species, breed, weight, and age. We believe that it is reasonable to conduct experimental trials devoted to investigation of spine aging processes with the help of morphometric data in animals, since they might be common factors in development of degenerative-dystrophic changes in humans and some groups of animals and as the result they could be predictors of ageing of an organism as a whole. Such kind of clinical and morphometric comparative characteristics between humans and domestic animals can form the basis of modeling prevention methods for premature aging in humans.

Conclusions

Pathological deformations of the cervical spine were registered in 34.7% of animals, mainly in the form of straightened lordosis. The cervical spine configuration in cats and small breeds of dogs was more often preserved than in large breeds of dogs. Such changes were significant and significantly exceeded the same indexes in the other groups of animals. Only large breeds of dogs had the similar spine deformations to those in humans.

The C₃ vertebra density measurements in patients with degenerative-dystrophic processes of the cervical spine failed to reveal pathological changes. Comparative C₃ vertebra measurements with the deformed C₅–C₇ (C₆) vertebrae, which were the “peak” of pathological lordosis, indicate significant changes as a result of dynamic loading. Similar changes were registered only in large breeds of dogs. The density of vertebral bodies in all groups decreased in the cervical spine caudal direction. The difference was maximal in humans as well as in large breeds of dogs in which these indexes approached the same in humans.

Degenerative-dystrophic changes in the cervical spine in humans were observed not only in old age but also in young and middle age. Despite the same age range of the studied groups, such a tendency was found only in large breeds of dogs.

Therefore, the revealed regularities of morphometric and clinical analysis of degenerative-dystrophic changes in the cervical spine indicate that large breed dogs can be model for studying etiopathogenetic factors, clinical course, prognosis and other risks of degeneration of the bone-cartilage apparatus at the cervical level in humans. Such kind of clinical and morphometric comparative characteristics between humans and domestic animals can form the basis of methods of modeling the prevention of premature aging in humans.

This study was supported in parts by the funds of the target program “Improving the prevention and treatment of the main eco-dependent and occupationally caused diseases based on the study of the peculiarities of their etiology and pathogenesis” of the Ministry of Health of Ukraine (state registration No. 0116U008822) and the grant support “Determination of the Torg-Pavlov index during computed tomographic examination of people and animals” (state registration No. 0123U102036).

The authors declare that they have no conflict of interest.

References

Adamovych, O. O. (2016). Porivniannia liniynykh rozmiriv ta schil'nosti struktur shyjnoho viddilu khrebtu u osib riznoji stati [Comparison of linear dimensions and density of structures of the cervical spine in individuals of different sexes]. *Herald of Problems of Biology and Medicine*, 128, 302–305 (in Ukrainian).

Adams, J. E. (2009). Quantitative computed tomography. *European Journal of Radiology*, 71(3), 415–424.

Afanasyev, S. M., & Maikova, T. V. (2017). Efektyvnist' fizychnoji reabilitaciji pry poperekovo-kryzhovomu osteochondrozi, pobudovanoi na pidgrunni osteogennoi koncepciji rozvytku zakhvoriuvannya [The effectiveness of physical rehabilitation in lumbosacral osteochondrosis, built on the basis of the osteogenic concept of the development of the disease]. *Scientific Journal of the National Pedagogical University named after M. P. Drahomanov*, 11, 8–13 (in Ukrainian).

Anderst, W. J., Thorhauer, E. D., Lee, J. Y., Donaldson, W. F., & Kang, J. D. (2011). Cervical spine bone mineral density as a function of vertebral level and anatomic location. *The Spine Journal*, 11(7), 659–667.

Baba, H., Uchida, K., Maezawa, Y., Furusawa, N., Azuchi, M., & Imura, S. (1996). Lordotic alignment and posterior migration of the spinal cord following en bloc

open-door laminoplasty for cervical myelopathy: A magnetic resonance imaging study. *Journal of Neurology*, 85, 626–632.

Been, E., Shefi, S., & Soudack, M. (2017). Cervical lordosis: The effect of age and gender. *The Spine Journal*, 17(6), 880–888.

Bland, J. H., & Boushey, D. R. (1990). Anatomy and physiology of the cervical spine. *Seminars of Arthritis and Rheumatism*, 20(1), 1–20.

Bohndorf, K. (1998). Osteochondritis (osteochondrosis) dissecans: A review and new MRI classification. *European Radiology*, 8(1), 103–112.

Ezra, D., Kalichman, L., Simonovich, A., Droujin, J., Been, E., & Alperovitch-Najenson, D. (2020). The association between cervical lordosis and age, sex, history of cervical trauma and sedentarity: ACT study. *Archives of Anatomy and Physiology*, 5(1), 9–15.

Gloth, F. M., Scheve, A. A., Stober, C. V., Chow, S., & Prosser, J. (2001). The functional pain scale: Reliability, validity, and responsiveness in an elderly population. *Journal of the American Medical Directors Association*, 2(3), 110–114.

Harrison, D. E., Cailliet, R., Harrison, D. D., Janik, T. J., & Holland, B. (2002). A new 3-point bending traction method for restoring cervical lordosis and cervical manipulation: A nonrandomized clinical controlled trial. *Archives of Physical Medicine and Rehabilitation*, 83(4), 447–453.

Hernandez-Avalos, I., Mota-Rojas, D., Mora-Medina, P., Martínez-Bumes, J., Alvarado, A. C., Verduzco-Mendoza, A., Lezama-García, K., & Olmos-Hernández, A. (2019). Review of different methods used for clinical recognition and assessment of pain in dogs and cats. *International Journal of Veterinary Science and Medicine*, 7(1), 43–54.

Hjelm-Björkman, A. K., Kapatkin, A. S., & Rita, H. J. (2011). Reliability and validity of a visual analogue scale used by owners to measure chronic pain attributable to osteoarthritis in their dogs. *American Journal of Veterinary Research*, 72(5), 601–607.

Hussein, A. I., Jackman, T. M., Morgan, S. R., Barest, G. D., & Morgan, E. F. (2013). The intravertebral distribution of bone density: Correspondence to intervertebral disc health and implications for vertebral strength. *Osteoporosis International*, 24(12), 3021–3030.

Kawakami, M., Tamaki, T., Yoshida, M., Hayashi, N., Ando, M., & Yamada, H. (1999). Axial symptoms and cervical alignments after cervical anterior spinal fusion for patients with cervical myelopathy. *Journal of Spinal Disorders*, 12, 50–56.

Kharchenko, Y. A. (2014). Adekvatnaja otsenka boli – zalog jejo uspehnogo lechenija [An adequate assessment of pain is the key to its successful treatment]. *Universum: Medicine and Pharmacology*, 4(5), 4 (in Russian).

Mann, V., & Ralston, S. H. (2003). Meta-analysis of COL1A1 Sp1 polymorphism in relation to bone mineral density and osteoporotic fracture. *Bone*, 32, 711–717.

Mathews, K., Kronen, P. W., Lascelles, D., Nolan, A., Robertson, S., Steagall, P. V., Wright, B., & Yamashita, K. (2014). Guidelines for recognition, assessment and treatment of pain. *Journal of Small Animal Practice*, 55(6), e10–e68.

McAviney, J., Schulz, D., Bock, R., Harrison, D. E., & Holland, B. (2005). Determining the relationship between cervical lordosis and neck complaints. *Journal of Manipulative and Physiological Therapeutics*, 28, 187–193.

Mikhailov, A. N., & Abelskaya, I. S. (2015). Sravnitelnyj analiz znachimosti metodov luchevoj diagnostiki pri kharakteristike kostnykh struktur pozvonochnykh segmentov pri shejnom osteochondroze [Comparative analysis of the significance of radiological diagnostic methods in the characterization of bone structures of vertebral segments in cervical osteochondrosis]. *International Reviews: Clinical Practice and Health*, 4, 5–6 (in Russian).

Morales-Avalos, R., Leyva-Villegas, J., Sánchez-Mejorada, G., Cárdenas-Sema, M., Vilchez-Cavazos, F., Martínez-Ponce De León, A., Elizondo-Riojas, G., Martínez-García, J., De La Garza-Castro, O., Elizondo-Omaña, R., & Guzmán-López, S. (2013). Age- and sex-related variations in morphometric characteristics of thoracic spine pedicle: A study of 4,800 pedicles. *Clinical Anatomy*, 27(3), 441–450.

Nightingale, R. W., McElhaney, J. H., Richardson, W. J., Best, T. M., & Myers, B. S. (1996). Experimental impact injury to the cervical spine: Relating motion of the head and the mechanism of injury. *Journal of Bone and Joint Surgery*, 78, 412–421.

Nurmieva, C. R., & Bogdanov, E. I. (2011). Cervical spinal stenosis: Clinical forms, diagnostic criteria and treatment. *Neurology Bulletin*, 48(4), 57–64.

Patel, P. D., Arutyunyan, G., Plusch, K., Vaccaro Jr., A., & Vaccaro, A. R. (2020). A review of cervical spine alignment in the normal and degenerative spine. *Journal of Spine Surgery*, 6(1), 106–123.

Pavlova, S. V., Avrunina, O. G., Zlepka, V., & Bodyanskyi, E. V. (2019). Intelektual'ni tekhnolohiji v medychnij diahnostytsi, likuvanni ta reabilitaciji [Intelligent technologies in medical diagnosis, treatment and rehabilitation]. *TD Edelweiss and K, Vinnytsia* (in Ukrainian).

Ravindra, V. M., Senglaub, S. S., Rattani, A., Dewan, M. C., Härtl, R., Bisson, E., Park, K. B., & Shrimme, M. G. (2018). Degenerative lumbar spine disease: Estimating global incidence and worldwide volume. *Global Spine Journal*, 8(8), 784–794.

Riggs, B. L., & Melton, L. J. (1995). The worldwide problem of osteoporosis: Insights afforded by epidemiology. *Bone*, 17, 505–511.

Rupp, R. (2020). Spinal cord lesions. *Handbook of Clinical Neurology*, 168, 51–65.

- Stein, J. (1997). Failure of magnetic resonance imaging to reveal the cause of a progressive cervical myelopathy related to postoperative spinal deformity: A case report. *American Journal of Physical Medicine and Rehabilitation*, 76, 73–75.
- Stoyanov, A. N., Vastyanov, R. S., & Skorobreha, V. Z. (2015). Patofiziologicheskiye mekhanizmy nejrovegetologii boli [Pathophysiological mechanisms of neurovegetology of pain]. Astro-Print, Odessa (in Russian).
- Swank, M. L., Sutterlin, C. E., Bossons, C. R., & Dials, B. E. (1997). Rigid internal fixation with lateral mass plates in multilevel anterior and posterior reconstruction of the cervical spine. *Spine*, 22, 274–282.
- Teo, A. Q. A., Thomas, A. C., & Hey, H. W. D. (2020). Sagittal alignment of the cervical spine: Do we know enough for successful surgery? *Journal of Spine Surgery*, 6(1), 124–135.
- Tjahjadi, D., & Onibala, M. Z. (2010). Torg ratios based on cervical lateral plain films in normal subjects. *Universal Medicine*, 29, 8–10.
- Wang, T., Ma, J., Hogan, A. N., Fong, S., Licon, K., Tsui, B., Kreisberg, J. F., Adams, P. D., Carvunis, A. R., Bannasch, D. L., Ostrander, E. A., & Ideker, T. (2020). Quantitative translation of dog-to-human aging by conserved remodeling of the DNA methylome. *Cell Systems*, 11(2), 176–185.
- Yates, K. (2021). *The math of life and death: 7 mathematical principles that shape*. Scribner.
- Yemecz, O. T., Maxlynech, V. Y., Vansovych, O. S., Sapiga, I. I., & Oros, M. M. (2020). Cervikalgiya: Suchasni pidkhody do likuvannia [Cervicalgia: Modern approaches to treatment]. *International Journal of Neurology*, 16(4), 50–54 (in Ukrainian).