TITLE: Caudal articular process dysplasia of thoracic vertebrae in neurologically normal French bulldogs, English bulldogs, and Pugs: Prevalence and characteristics

AUTHORS: Bertram, S; Ter Haar, G; De Decker, S

JOURNAL: VETERINARY RADIOLOGY & ULTRASOUND

PUBLISHER: Wiley

PUBLICATION DATE: 20 February 2018 (online)

DOI: https://doi.org/10.1111/vru.12609

Caudal Articular Process Dysplasia of Thoracic Vertebrae in Neurologically Normal French Bulldogs, English Bulldogs and Pugs: Prevalence and Characteristics

Simon Bertram[1], Gert ter Haar[1,2], Steven De Decker[1]

[1]Department of Clinical Science and Services, Royal Veterinary College, University of London, Hatfield, UK; [2]Specialistische Dierenkliniek Utrecht, Utrecht, the Netherlands

Address of Corresponding author: Simon Bertram; Queen Mother Hospital for Animals (QMHA), The Royal Veterinary College, Hawkshead Lane, North Mymms, Hatfield, Hertfordshire, AL9 7TA, United Kingdom; sbertram@rvc.ac.uk

Key Words: Brachycephalic, Vertebral malformation, Facet joint

Running head: Thoracic Caudal Articular Process Dysplasia

16 Abstract

17

18 The aims of this study were to evaluate the prevalence and anatomical characteristics of
19 thoracic caudal articular process dysplasia in French bulldogs, English bulldogs and Pugs
20 presenting for problems unrelated to spinal disease.
21 In this retrospective cross-sectional study, computed tomography scans of the thoracic
22 vertebral column of these three breeds were reviewed for the presence and location of caudal
23 articular process hypoplasia and aplasia and compared between breeds.
24 A total of 271 dogs met the inclusion criteria: 108 French bulldogs, 63 English bulldogs and
25 100 Pugs. 70.4% of French bulldogs, 84.1% of English bulldogs and 97.0% of Pugs showed
26 evidence of caudal articular process dysplasia. Compared to French and English bulldogs,
27 Pugs showed a significantly higher prevalence of caudal articular process aplasia, but also a
28 lower prevalence of caudal articular process hypoplasia, a higher number of affected
29 vertebrae per dog and demonstrated a generalized and bilateral spatial pattern more
30 frequently. Furthermore, Pugs showed a significantly different anatomical distribution of
31 caudal articular process dysplasia along the vertebral column with a high prevalence of
32 caudal articular process aplasia between T10 and T13. This area was almost completely
33 spared in French and English bulldogs.
34 As previously suggested, caudal articular process dysplasia is a common finding in
35 neurologically normal Pugs but this also seems to apply to French and English bulldogs. The
36 predisposition of clinically relevant caudal articular process dysplasia in Pugs is possibly not
37 only caused by the higher prevalence of caudal articular process dysplasia but also by the
38 breed specific anatomical characteristics.

Introduction

The cranial and caudal vertebral articular processes are located at the junction of the vertebral pedicle and lamina. Together they form the synovial facet or zygapophysial joint which together with the intervertebral discs are an important part of each functional spinal unit. Their main function is to provide stability and restrict motion. They contribute up to 30% of the stability of the vertebral column.[1, 2] A complete (aplasia) or partial (hypoplasia) absence of articular processes is defined as vertebral articular process dysplasia[3] which is considered a congenital vertebral anomaly in the majority of documented cases.[4-10]

Whereas dysplasia of the cranial articular process seems very rare, dysplasia of the caudal articular process is well-documented.[3] Although multiple dog breeds can be affected[4, 6, 9] Pugs seem especially vulnerable for this condition with an anatomical predisposition for the thoracic vertebral column.[5, 10, 11] Caudal articular process dysplasia can be associated with progressive signs of spinal cord dysfunction,[3, 5, 11] including paraparesis, ataxia of the pelvic limbs and urinary incontinence. Caudal articular process dysplasia can however occur in neurologically normal dogs and recent research abstracts have indicated a prevalence of more than 60% in neurologically normal Pugs and Pug crosses.[10, 11] It has further been suggested that only 4% of Pugs diagnosed with caudal articular process dysplasia will demonstrate neurological signs.[11] This is in agreement with the results of a recent study, which indicated that thoracic vertebral malformations occur commonly in neurologically normal "screw-tailed" brachycephalic dog breeds, such as Pugs, French bulldogs and English bulldogs.[12] This high prevalence of vertebral malformations in neurologically normal dogs is clinically important. Failure to recognize that vertebral malformations can be clinically irrelevant could cause delay in reaching an accurate diagnosis and postpone initiation of appropriate treatment in "screw-tailed" brachycephalic dogs with spinal disease. It is further unclear why most dogs

with vertebral malformations are clinically unaffected, while some dogs develop progressive and debilitating clinical signs. If we want to increase our understanding about the pathophysiology of vertebral malformations, it can be considered an important first step to understand the prevalence and spectrum of such anomalies in clinically unaffected dogs. The aims of this study were therefore to evaluate the prevalence and anatomical characteristics of caudal articular process dysplasia in French bulldogs, English bulldogs and Pugs presenting for problems unrelated to spinal disease. It was hypothesized that caudal articular process dysplasia would be common in all three evaluated breeds and that breed specific differences would exist in prevalence and anatomical location of such anomalies.

Material and Methods

This retrospective descriptive cross-sectional study was approved by the Clinical Research Ethical Review Board of the Royal Veterinary College, University of London (URN 2017 1689-1). The electronic medical database of the Small Animal Referral Hospital, Royal Veterinary College was searched for French bulldogs, English bulldogs and Pugs which underwent computed tomography (CT), including the complete thoracic vertebral column, for reasons unrelated to a spinal disease, from October 2010 to November 2016. Dogs were included if the medical files and CT studies were available for review. Dogs were excluded if a neurological or orthopaedic disease was the cause for investigation, if the CT studies were not available for review or if the CT studies did not include the complete thoracic vertebral column. This decision was made by the first author (S.B., Veterinary specialist-in-training in Veterinary Neurology and Neurosurgery).

Information retrieved from the medical files included signalment, presenting clinical signs and final diagnosis. CT images were reviewed by one investigator (S.B., under direct supervision of a board-certified neurologist, S.D.D.) in a randomized order using a random sequence generator (random.org) and blinded to any patient data. The investigator was aware that none of the included dogs had recorded orthopaedic or neurological signs. After retrieval from PACS to a workstation (MacBook Pro 13 inch, 2015, Apple Inc.) a commercially available DICOM viewing software (Horos, version 1.1.7., www.horosproject.org) was used. After transverse images were obtained, multiplanar sagittal and dorsal reconstructions as well as 3D reconstructions were made and reviewed. The vertebrae from T1 to the last true thoracic vertebra were individually and bilaterally assessed for presence of aplasia (complete absence) or hypoplasia (incomplete formation) of the caudal articular process (Fig. 1 and 3).[3, 5]

The occurrence, number and location of hypoplastic and aplastic vertebral caudal articular processes were recorded and compared between breeds. To enable further comparisons included dogs were assigned to one group of two categories of CT characteristics by the investigator (S.B.). The first category considered presence of caudal articular process hypoplasia and aplasia. Dogs lacking any signs of caudal articular process hypoplasia or aplasia were considered "unaffected" and dogs demonstrating caudal articular process hypoplasia or aplasia were assigned to the group "caudal articular process dysplasia". The latter group was furthermore subdivided into the groups "caudal articular process hypoplasia" (articular process hypoplasia without articular process aplasia) and "caudal articular process aplasia" (articular process aplasia with or without articular process hypoplasia). In the second category, the spatial distribution of the abnormalities was evaluated for the dogs with caudal articular process dysplasia. Dogs were assigned to one of the three following groups by the investigator (S.B.): focal (only one region of affected adjacent vertebrae, < 7 affected vertebrae overall), multifocal (multiple regions of affected adjacent vertebrae, < 7 affected vertebrae overall) or generalised (> 7 affected vertebrae overall) (Table. 1).

Data was recorded using a spreadsheet (Microsoft Excel for Mac, Version 15.33). Statistical tests were performed by the first author (S.B.) and a statistical analysis software (SPSS Statistics for OSx, Version 24.0, IBM Corp, Armonk, NY) was used to analyse the data. Data was tested for normal distribution to enable selection of the correct statistical test using a Kolmogorov-Smirnov test. Interaction between the occurrence of abnormalities in the different breeds at each vertebral level was tested using a generalized estimating equation to account for the repeated measures from the same dog (logistic link function and exchangeable correlation matrix was implemented). Interbreed differences between the occurrence of abnormalities at each individual vertebral level and the general lesion patterns were tested using Fisher's Exact test corrected for multiple comparison according to

Bonferroni. A binary logistic regression model was used to test age and sex as covariates for the breed specific prevalence of articular process hypoplasia and aplasia. For comparison of the number of affected vertebrae between breeds Kruskal-Wallis test and post hoc multiple comparison with Bonferroni correction was applied. Statistical significance was defined as $P < 0.05$.

Results

Included animals

A total of 271 dogs were included in the study, consisting of 108 French bulldogs, 63 English bulldogs and 100 Pugs. Included animals underwent CT imaging for a variety of reasons, including brachycephalic obstructive airway syndrome (n = 207), other respiratory disease, neoplastic disease (n = 17 for both), gastrointestinal disease (n = 13), trauma (n = 7), cardiac disease and ear disease (n = 5 for both). All CT scans were acquired using a 16-slice scanner (Mx8000 IDT, Philips, Best, The Netherlands) with dogs in sternal recumbency under anaesthesia or sedation. Following parameters were used: 16 × 1.5 mm collimation, helical scan mode, 2 or 3 mm reconstruction slice thickness with 1 to 1.5 mm overlap, 2s tube rotation time, 120 to 180 mA depending on patient size, 120 to140 kVp, 500 mm acquisition field of view, with reconstruction field of view dependent on patient body size (varying between 200–250 mm), and 512×512 matrix.

Overall, 226 of 271 dogs (83.39%) and 1104 of 3506 (31.49%) vertebrae demonstrated thoracic caudal articular process dysplasia. More specifically, 198 of 271 dogs (73.06%) and 476 of 3506 (13.58%) vertebrae demonstrated caudal articular process hypoplasia of which 42 of 271 dogs (15.50%) exclusively showed caudal articular process hypoplasia. 184 of 271 dogs (67.89%) and 628 of 3506 (17.91%) vertebrae demonstrated aplasia of the caudal articular process (Fig. 1 and 2).

The group of 108 French bulldogs consisted of 79 males (27 neutered) and 29 females (10 neutered), aged between three and 133 months old (median 18 months). All dogs of this breed had 13 thoracic vertebrae. 76 of 108 of French bulldogs (70.4%) showed dysplasia, 29 of 108 (26.9%) showed hypoplasia and 47 of 108 (43.5%) showed caudal articular process

aplasia (Table. 1). In 56 of the 76 (85.5%) affected dogs, multiple vertebrae demonstrated caudal articular process dysplasia. Of the 1404 evaluated vertebrae, 224 (16.0%) demonstrated caudal articular process dysplasia (of which 147 showed hypoplasia and 77 aplasia). A focal spatial pattern was seen in 27 (35.5%) French bulldogs, a multifocal pattern in 45 (59.2%) and a generalised pattern in four of 76 dogs (5.3%). In five (8.9%) of the 56 dogs which had multiple affected vertebrae, caudal articular process dysplasia was seen on one side of the vertebral column only. In the remaining 51 dogs (91.1%), caudal articular process dysplasia was seen on both sides of the vertebral column. Finally, 87 of 224 (38.8%) of the vertebrae showing dysplasia of the caudal articular process were affected bilateral. In French bulldogs with caudal articular process aplasia, T9 (17 of 77 vertebrae (22.1%)) was most often affected followed by T4 (16 of 77 vertebrae (20.8%)) (Fig. 3). Hypoplasia was most often observed at T10 (22 of 147 vertebrae (15.0%)) followed by T11 (18 of 147 vertebrae (12.2%)).

The group of 63 English bulldogs consisted of 39 males (nine neutered) and 24 females (eight neutered), aged between three and 132 months old (median 14 months). All dogs of this breed had 13 thoracic vertebrae. 53 of 63 of English bulldogs (84.1%) showed dysplasia, 12 of 63 (19.0%) showed hypoplasia and 41 of 63 (65.1%) showed caudal articular process aplasia. In 40 of the 53 (75.5%) affected dogs, multiple vertebrae demonstrated caudal articular dysplasia. Of the 819 evaluated vertebrae, 193 (23.6%) demonstrated caudal articular process dysplasia (of which 116 showed hypoplasia and 77 aplasia). A focal spatial pattern was seen in 22 (41.5%) English bulldogs, a multifocal pattern in 23 (43.5%) and a generalised pattern in eight of 53 dogs (15.0%). In 10 (25.0%) of the 40 dogs which had multiple affected vertebrae, caudal articular process dysplasia was seen on one side of the vertebral column only. In the remaining 30 dogs (75.0%), caudal articular process dysplasia was seen on both sides of the vertebral column. Finally, 60 of 193 (31.1%) of the vertebrae

178 showing dysplasia of the caudal articular process were affected bilateral. In English bulldogs
179 with caudal articular process aplasia, T4 (16 of 77 vertebrae (20.8%)) was most often
180 affected followed by T9 (15 of 77 vertebrae (19.5%)) (Fig. 3). Hypoplasia was most often
181 observed at T10 (20 of 116 vertebrae (17.2%)) followed by T11 (14 of 116 vertebrae
182 (12.1%)).
183 The group of 100 Pugs consisted of 54 males (24 neutered) and 46 females (29 neutered),
184 aged between seven and 151 months old (median 31.5 months). 17 of the 100 pugs (17.0%)
185 had only 12 thoracic vertebrae. 97 of 100 of Pugs (97.0%) showed dysplasia, one of 100
186 (1.0%) showed hypoplasia and 96 of 100 (96.0%) showed caudal articular process aplasia. In
187 94 of the 97 affected dogs (96.9%), multiple vertebrae demonstrated caudal articular
188 dysplasia. Of the 1283 evaluated vertebrae, 687 (53.5%) demonstrated caudal articular
189 process dysplasia (of which 216 showed hypoplasia and 471 aplasia). A focal spatial pattern
190 was seen in nine (9.3%) Pugs, a multifocal pattern in 33 (34.0%) and a generalised pattern in
191 55 of 97 dogs (56.7%). In two (2.1%) of the 94 dogs which had multiple affected vertebrae,
192 caudal articular process dysplasia was seen on one side of the vertebral column only. In the
193 remaining 92 dogs (97.9%), caudal articular process dysplasia was seen on both sides of the
194 vertebral column. Finally, 484 of 687 (70.4%) of the vertebrae showing dysplasia of the
195 caudal articular process were affected bilateral. In Pugs with caudal articular process aplasia,
196 T10 (65 of 471 vertebrae (13.8%)) was most often affected followed by T3 ((56 of 471
197 vertebrae (11.9%)), T11 and T12 (51 of 471 vertebrae (10.8%)) (Fig. 3). Hypoplasia was
198 most often observed at T4 (28 of 216 vertebrae (13.0%)) followed by T9 (26 of 216 vertebrae
199 (12.0%)).
200
201 *Comparison between breeds*
202

Breed had a significant influence on the prevalence of thoracic caudal articular process dysplasia ($P < 0.0001$) whereas age and sex had not ($P > 0.05$). More specifically, Pugs were more often affected compared to French bulldogs ($P < 0.0001$, OR = 13.6 95% CI [4.0, 46.2]) and English bulldogs ($P < 0.05$, OR = 6.13 95% CI [1.64, 23.1]). There was no significant difference between French and English bulldogs ($P > 0.05$). Breed also had a significant influence on the prevalence of thoracic caudal articular process hypoplasia and aplasia ($p < 0.0001$ for both) whereas age and sex had not ($P > 0.05$). Pugs were significantly less often affected by hypoplasia and more often affected by aplasia compared to French (hypoplasia: $P < 0.0001$, OR = 0.028 95%, CI [0.004, 0.206]; aplasia: $P < 0.0001$, OR = 31.2, 95% CI [10.7, 90.8]) and English bulldogs (hypoplasia: $P < 0.0001$, OR = 0.043, 95% CI [0.005, 0.339]; aplasia: $P < 0.0001$, OR = 12.9, 95% CI [4.23, 39.7]). There was no significant difference between French and English bulldogs concerning hypoplasia ($P > 0.05$) but English bulldogs were more often affected by aplasia compared to French bulldogs ($P < 0.05$, OR = 2.42, 95% CI [1.25, 4.61]). Pugs had a significantly ($P < 0.001$) higher number of vertebrae affected per dog by thoracic caudal articular process dysplasia (median 7, IQR 5-10) compared to French (median 2, IQR 0-3) and English bulldogs (median 3, IQR 1-5). There was no significant difference between French and English bulldogs ($P > 0.05$).

Pugs showed significantly more often a generalised spatial pattern of thoracic caudal articular process dysplasia compared to French ($P < 0.0001$) and English bulldogs ($P < 0.0001$). There was no significant difference between French and English bulldogs ($P > 0.05$). Multiple vertebrae were affected by thoracic caudal articular process dysplasia significantly more often in Pugs compared to French ($P < 0.0001$) and English bulldogs. If more than one vertebra was affected, thoracic caudal articular process dysplasia was confined to only one side significantly more often in English bulldogs compared Pugs ($P < 0.001$). There was no significant difference between French bulldogs and Pugs ($P > 0.05$) and French and English

bulldogs ($P > 0.05$). Furthermore, Pugs had a significantly higher number of vertebrae affected by bilateral thoracic caudal articular process dysplasia compared to French ($P < 0.0001$) and English bulldogs ($P < 0.0001$). There was no significant difference between French and English bulldogs ($P > 0.05$).

Breed had a significant influence on the anatomical distribution of caudal articular process hypoplasia ($P < 0.01$) and aplasia ($P < 0.001$) along the thoracic vertebral column. More specifically, T4 and T9 in French and English bulldogs and T5 in English bulldogs were significantly more often affected by caudal articular processes aplasia compared to Pugs (P values < 0.01). In Pugs T10, T11 and T12 were significantly more often affected by caudal articular processes aplasia compared to French and English bulldogs ($P < 0.05$, $P < 0.01$ and $P < 0.001$ respectively). There was no significant difference between French and English bulldogs ($P > 0.05$). Overall, 40.4% of the vertebrae showing caudal articular processes aplasia in Pugs were located between T10 and T13 compared to 11.6% and 5.2% in French and English bulldogs, respectively (Fig. 3, 4 and 5).

Moreover, T4 was significantly more often affected in Pugs compared to French bulldogs ($P < 0.05$) and T10 was significantly less often affected by caudal articular processes hypoplasia in Pugs compared to French and English bulldogs (P values < 0.01). There was no significant difference between French and English bulldogs ($P > 0.05$). Overall, 25.9% of the vertebrae showing caudal articular processes hypoplasia in Pugs were located between T10 and T13 compared to 42.2% and 42.9% in French and English bulldogs, respectively.

Discussion

This study evaluated and compared thoracic caudal articular process dysplasia in three "screw-tailed" brachycephalic dog breeds. Our results did not only demonstrate a very high prevalence of caudal articular process dysplasia in Pugs (97.0%) presenting for problems unrelated to spinal disease, but additionally in French (70.4%) and English bulldogs (84.1%) which, to the authors knowledge, has not been reported previously.

Compared to the suggested prevalence in previously published research abstracts of caudal articular process dysplasia in Pugs presenting for problems unrelated to spinal disease, which were 64.4% and 76.2%, the prevalence in this study was remarkably higher.[10, 11] Although other reasons cannot be excluded, this discrepancy could possibly be explained by differences in the chosen imaging modality. In one study, dogs underwent mainly survey radiographs,[12] while in the other study dogs underwent a combination of magnetic resonance imaging (MRI) and survey radiographs.[11] Cross sectional imaging techniques and especially CT scans enable a more detailed evaluation of small changes in bony structures compared to radiographs.[3]

Thoracic caudal articular process dysplasia has been considered a breed-specific disorder in Pugs.[5, 10, 11] The results of this study show that not only Pugs have a high prevalence of caudal articular process dysplasia but that this seems to be also true for other brachycephalic "screw-tailed" breeds. If compared to French and English bulldogs Pugs showed a significantly higher prevalence of caudal articular process dysplasia, a significantly higher number of affected vertebrae per dog, Pugs had significantly more often caudal articular process aplasia, significantly less often hypoplasia, demonstrated significantly more frequently a generalized spatial pattern and vertebra being affected bilateral. Furthermore, Pugs showed a significantly different anatomical distribution of caudal articular process dysplasia along the vertebral column with a high prevalence of articular process aplasia

between T10 and T13. This area was almost completely spared in the two other breeds (Fig. 3 and 5).

Although the exact mechanism is currently unknown, there are multiple hypotheses about the pathogenesis of articular process dysplasia. It is generally accepted that a failure of ossification in the neural arch ossification center leads to a failure of articular process formation.[13] A mutation of a Hox gene which plays a major regulatory role in chondrocytic proliferation and differentiation,[5, 6] dysgenesis of the neural arch ossification centre itself[14] or a lack of development or union of an accessory ossification centre with the lamina are considered possible underlying mechanisms.[9, 14, 15]

It is currently unclear why only a minority of dogs with caudal articular process dysplasia will develop clinical signs of spinal cord dysfunction, while this vertebral anomaly seems to be an incidental finding in the majority of affected dogs. It is further unclear why this vertebral anomaly has been associated with clinical disease especially in Pugs,[5] while the results of this study suggest also a high prevalence in other "screw-tailed" brachycephalic dogs. It can be hypothesised that the high prevalence of caudal articular process dysplasia should not be considered the only factor causing a predisposition of clinical disease in Pugs.

It has been proposed that hypoplasia and especially aplasia of the caudal articular process can result in instability of the vertebral column[2, 3, 16] whereby the location of the defect is thought to be of importance due to the regionally differing biomechanical properties of the facet joints.[13] This could be of importance when trying to explain why Pugs seem to be more prone to suffer from clinical sequelae compared to other breeds.

Depending on the segmental location the synovial facet joints contribute up to 30% of the stability of the vertebral column.[1, 2] The degree of motion of the different partition of the vertebral column is dictated by the differing orientation of the caudal and cranial articular processes to each other.[3] The more opposing the incline of articulation, the higher is the

achieved stability.[13] Based on the differing anatomical and biomechanical characteristics of the vertebral column and especially the facet joints, the thoracic vertebral column can be divided into a cranial (T1 to T9) and a caudal compartment (T11 to T13) which is separated by the diaphragmatic vertebra T10. The cranial thoracic vertebral column shows a very similar anatomy with the facet joints between T3 and T9 being almost confluent in the median plane with a horizontal orientation overlapping each other in a loft tile manner.[3, 4] Based on their arrangement the facet joints in this region do not play a major role in restricting motion but are suspected to have mainly weight bearing functions.[3, 4] Another important difference compared to the caudal thoracic vertebral compartment is the presence of the costovertebral joints, which provide a high degree of stability against axial rotation and lateral bending.[17] Overall, this part of the vertebral column is very rigid with the facet joins having mainly weight bearing and little stabilizing functions.

The diaphragmatic vertebra T10 and the anticlinal space between T10 and T11 have a unique anatomical conformation with a very high degree of opposing angles of the articular processes leading to a very high degree of stability.[3] The adjacent caudal thoracic vertebral column between T11 and T13 resembles the lumbar vertebrae with the articular processes being almost vertically aligned.[3, 18] Their main function is restricting lateral flexion and axial rotation making them an important stabilizing factor.[3, 6, 19, 20]Additionally to that they are also involved in weight bearing and the transmission of loading forces.[3, 20]. Therefore, this part of the vertebral column shows a higher degree of flexibility with the facet joints playing a very important part in restriction of excessive motion compared to the cranial thoracic compartment.

A lack of normal functioning facet joints, such as in caudal articular process dysplasia, is thought to cause a regional instability of the vertebral column. Furthermore, it can be hypothesized that an association exists between the degree of regional instability and the

degree of regional caudal articular process dysplasia. This would suggest that Pugs, which show a higher prevalence of caudal articular process aplasia, bilaterally affected vertebrae and a more generalized pattern often affecting multiple adjacent vertebrae would suffer from a higher degree of vertebral column instability compared to the other two investigated breeds. The different anatomical distribution of aplasia in Pugs could be an even more important difference. Due to the discussed anatomical and biomechanical differences, articular process aplasia of the caudal compartment of the thoracic vertebral column can be hypothesized to cause greater instability compared to the same defect in the cranial thoracic compartment (Fig. 4 and 5). The results of this study have shown an up to 8fold higher prevalence of articular process aplasia between T10 and T13 in Pugs affected by caudal articular process aplasia compared to affected French or English bulldogs (Fig. 3). It is therefore possible that this breed specific difference in the anatomical distribution of caudal articular process aplasia could be an important reason to explain the higher prevalence of clinical sequelae in Pugs. This hypothesis can be supported by a previous anatomic study looking at the incidence of articular process dysplasia in different large, chondrodystrophic and small non-chondrodystrophic breeds (eight Maltese and 27 Yorkshire Terriers).[4] Thoracic articular process dysplasia was exclusively detected in the examined Maltese and Yorkshire Terriers. The presented anatomical distribution was similar to that of French and English bulldogs in our study, with T11 to T13 being only affected in 6 to 14% of all of the examined Maltese and Yorkshire Terriers compared to 26 to 63% between T1 and T10.[4]

It has been hypothesized previously, that vertebral instability resulting from articular process dysplasia and a consequent increase in micromotion can lead to a condition termed fibrous constrictive myelopathy[5, 11] which has been well documented in Pugs[5, 21] and occasionally in other breeds.[6, 9, 21] The increase in motion results in the formation of a dense band of fibrotic tissue which can cause adhesions between the arachnoid and pia mater resulting in a

constriction of spinal cord.[5, 21] This condition clinically manifests as a slowly progressive myelopathy which is generally not painful and can be associated with urinary or fecal incontinence.[5] Treatment options for this disease include medical-palliative options, decompressive surgery which can be combined with vertebral stabilization or placement of a shunt tube bridging the site of constriction.[5, 21]

This study was limited by its retrospective design. While all dogs with a documented neurological abnormality where excluded from this study the majority of the included dogs did not underwent a neurological examination. Therefore, there is the probability that subtle gait abnormalities or neurological deficits where missed and we cannot exclude that the affected dogs could develop clinical signs later in life. Another limitation is that only three "screw-tailed" brachycephalic breeds were included in this study which makes it impossible to make any statements about the overall prevalence in the canine population. Additionally, this study was limited to CT scans with no MRI studies available for a detailed investigation of soft tissue structures and possible subtle myelopathies.

In conclusion, this study demonstrated that articular process dysplasia has not only a high prevalence in Pugs presenting for problems unrelated to spinal disease but also in two other "screw-tailed" brachycephalic breeds. It can be hypothesized that not only the higher prevalence but also the more generalized pattern and especially the high prevalence of this abnormality in the caudal thoracic vertebral column contribute to the predisposition of Pugs to develop clinical signs compared to the other two evaluated breeds. It is currently unknown why this very common abnormality is only rarely associated with development of clinical signs of spinal cord dysfunction. Further studies are therefore needed to investigate this abnormality in different breeds and to compare imaging findings of neurological normal and abnormal Pugs.

373 List of Author Contributions

374

375 Category 1

376 (a) Conception and Design: Steven De Decker, Gert ter Haar and Simon Bertram

377 (b) Acquisition of Data: Simon Bertram

378 (c) Analysis and Interpretation of Data: Simon Bertram

379

380 Category 2

381 (a) Drafting the Article: Simon Bertram and Steven De Decker

382 (b) Revising Article for Intellectual Content: Simon Bertram, Gert ter Haar and Steven De

383 Decker

384

385 Category 3

386 (a) Final Approval of the Completed Article: Simon Bertram, Gert ter Haar and Steven De

387 Decker

388 Acknowledgements

389

390 The authors thank Dr. Ruby Chang, Research Support Office, The Royal Veterinary College

391 for assistance with statistical analyses.

392 References

393

394 1. Hirsch C. The reaction of intervertebral discs to compression forces. J Bone Joint Surg Am
395 1955;37-A:1188-1196.

396 2. Smith GK, Walter MC. Spinal decompressive procedures and dorsal compartment injuries:
397 comparative biomechanical study in canine cadavers. Am J Vet Res 1988;49:266-273.

398 3. Bouma JL. Congenital Malformations of Vertebral Articular Processes in Dogs. Vet Clin
399 North Am Small Anim Pract 2016;46:307-326.

400 4. Breit S. Osteological and morphometric observations on intervertebral joints in the canine
401 pre-diaphragmatic thoracic spine (Th1–Th9). Vet J 2002;164:216-223.

402 5. Fisher SC, Shores A, Simpson ST. Constrictive myelopathy secondary to hypoplasia or
403 aplasia of the thoracolumbar caudal articular processes in Pugs: 11 cases (1993–2009). J Am
404 Vet Med Assoc 2013;242:223-229.

405 6. Werner T, McNicholas WT, Kim J, Baird DK, Breur GJ. Aplastic articular facets in a dog
406 with intervertebral disk rupture of the 12th to 13th thoracic vertebral space. J Am Anim Hosp
407 Assoc 2004;40:490-494.

408 7. Morgan JP. Congenital Anomalies of the Vertebral Column of the Dog: A Study of the
409 Incidence and Significance Based on a Radiographic and Morphologic Study. Vet Radiol
410 Ultrasound 1968;9:21-29.

411 8. Westworth DR, Sturges BK. Congenital spinal malformations in small animals. Vet Clin
412 North Am Small Anim Pract 2010;40:951-981.

413 9. Penderis J, Schwarz T, McConnell J, Garosi L, Thomson C, Dennis R. Dysplasia of the
414 caudal vertebral articular facets in four dogs: results of radiographic, myelographic and
415 magnetic resonance imaging investigations. Vet Rec 2005;156:601-605.

416 10. Full A, Dewey C, Bouma J. Prevelance And Magnetic Resonance Imaging Of
417 Intervertebral Disc Disease In Pugs With Caudal Articular Facet Dysplasia Of The
418 Thoracolumbar Spine. Vet Radiol Ultrasound 2014;55:681.

419 11. Ballegeer E, Patterson J, Pease A, Probst C. Incidence of vertebral anomalies in Pug
420 Dogs; Implications for myelopathies? Vet Radiol Ultrasound 2015;57:93.

421 12. Ryan R, Gutierrez-Quintana R, ter Haar G, De Decker S. Prevalence of thoracic vertebral
422 malformations in French bulldogs, Pugs and English bulldogs with and without associated
423 neurological deficits. Vet J 2017;221:25-29.

424 13. Evans HE. The skeleton: the vertebral column. In: Evans HE, editor. Miller's anatomy of
425 the dog. 3 ed. Philadelphia: WB Saunders Co; 1993. p. 166–181.

426 14. Rowe GG, Roche MB. The etiology of separate neural arch. J Bone Joint Surg Am
427 1953;35-A:102-110.

428 15. Rickenbacher J, Landolt AM, Theiler K. The Skeleton of the Back. In: Rickenbacher J,
429 Landolt AM, Theiler K, editors. Applied Anatomy of the Back 1ed. Berlin, Heidelberg:
430 Springer; 1985. p. 15-53.

431 16. Shires PK, Waldron DR, Hedlund CS. A biomechanical study of rotational stability in
432 unaltered and surgically altered canine thoracolumbar vertebral motion units. Prog Vet Neuro
433 1991;2:6-14.

17. Takeuchi T, Abumi K, Shono Y, Oda I, Kaneda K. Biomechanical role of the intervertebral disc and costovertebral joint in stability of the thoracic spine. A canine model study. Spine (Phila Pa 1976) 1999;24:1414-1420.

18. Hoerlein BF. Intervertebral disc protrusions in the dog. I. Incidence and pathological lesions. Am J Vet Res 1953;14:260-269.

19. Zimmerman MC, Vuono-Hawkins M, Parsons JR, Carter FM, Gutteling E, Lee CK, et al. The mechanical properties of the canine lumbar disc and motion segment. Spine (Phila Pa 1976) 1992;17:213-220.

20. Graichen H, Putz R. Anatomische und funktionelle Aspekte von Brust- und Lendenwirbelsäule. Manuelle Medizin 2006;44:479-486.

21. Meren IL, Chavera JA, Alcott CJ, Barker AK, Jeffery ND. Shunt tube placement for amelioration of cerebrospinal fluid flow obstruction caused by spinal cord subarachnoid fibrosis in dogs. Vet Surg 2017;46:289-296.

448 Tables

449

450 Table 1: Imaging Findings of Included Dogs

	French Bulldogs (n = 108)	**English Bulldogs (n = 63)**	**Pugs (n = 100)**
Evidence of caudal articular process			
dysplasia (%)	76 (70.4%)[1]	53 (84.1%)[3]	97 (97.0%)[1, 3]
hypoplasia (%)	29 (26.9%)[1]	12 (19.0%)[2]	1 (1.0%)[1, 2]
aplasia (%)	47 (43.5%)[1, 3]	41 (65.1%)[2, 3]	96 (96.0%)[1, 2]
Spatial pattern			
focal (%)	27 (35.5%)[3]	22 (41.5%)[1]	9 (9.3%)[1, 3]
multifocal (%)	45 (59.2%)	23 (43.4%)	33 (34.0%)
generalized (%)	4 (5.3%)[1]	8 (15.0%)[2]	55 (56.7%)[1, 2]

451 Note: Superscript letters indicate a statistical significant difference between two breeds ([1] and

452 [2] = $P < 0.0001$, [3] = $P < 0.01$)

453 Figure legends

454

455 Figure 1: Transverse CT images at the level of the T4/T5 facet joint showing the difference
456 between an anatomical correct facet joint (A,C), consisting of normally developed cranial
457 (arrow, red outline) and caudal (arrowhead, blue outline)) articular processes, and a case of
458 right sided unilateral caudal articular process aplasia (B,D).

459

460 Figure 2: Transverse CT images at the level of the T11/12 facet joint showing the difference
461 between an anatomical correct facet joint (A,C), consisting of normally developed cranial
462 (arrow, red outline) and caudal (arrowhead, blue outline) articular processes, and a case of
463 bilateral caudal articular process aplasia (B,D).

464

465 Figure 3: Spatial distribution of caudal articular process aplasia between T1 and T13. The
466 stated percentage is the number of dogs with caudal articular process aplasia at a specific
467 vertebra divided by the overall number of vertebra affected by articular process aplasia in this
468 breed (* $P < 0.05$, ** $P < 0.01$, *** $P < 0.001$).

469

470 Figure 4: 3D reconstructed CT study of the cranial (T1 to T7) thoracic vertebral column and
471 ribs with evidence of hypoplasia (arrowhead) and aplasia (arrows) of the caudal articular
472 processes of T2, T3 and T4. The caudal articular processes of T1, T5 and T6 are developed
473 normally (asterisks).

474

475 Figure 5: 3D reconstructed CT study of the caudal (T10 to T13) thoracic vertebral column
476 and ribs with evidence of hypoplasia (arrowhead) and aplasia (arrows) of the caudal articular
477 processes.