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ORIGINAL RESEARCH

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Presumed residual thymic tissue is a common finding in thoracic computed tomography in adult dogs

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Abstract

Residual thymic tissue is a common incidental finding in thoracic CT of human adults. To determine whether presumed residual thymic tissue is also a common incidental finding in adult dogs, a two part-study was performed. The first part was a prospective, descriptive design where CT examination was performed in six canine cadavers within 24 h after death and presumed residual thymic tissue was examined pathologically. The second part of the study was a retrospective, analytical design where medical records of our institution were searched for thoracic CT scans of adult dogs performed in the year 2020. Age, sex, breed, presence of presumed thymic tissue, location, shape, attenuation, homogeneity, and width of the tissue were recorded and comparisons were performed using these data. In 4 of 6 of the prospective cases, thymic tissue was present on histology and in 2 of 6 dogs the presence of thymic tissue could not be confirmed. For the retrospective study, in 161/169 (95.3%) cases with presumed residual thymic tissue were detected. Shape and size were highly variable with either homogeneous (46.6%), heterogeneous (42.9%), or mixed (10.6%) attenuation. Dogs with presumed residual thymic tissue were significantly younger (median: 9.1 years; range: 1.2–14.3 vs. median: 10.5 years; range: 9.4–12.3) as were dogs with homogeneous attenuation of the tissue (median: 8.1 years; range: 1.2–14.3 vs. median: 9.5 years; range: 4.0–14.3). In conclusion, results indicated that presumed residual thymic tissue is a common CT finding in adult dogs and can be considered incidental.

KEYWORDS
canine, mediastinal, thymic remnant, thymus

1 | INTRODUCTION

The cranial mediastinum is a common location for pathology in dogs.[1,2] The authors have encountered a wide variation in the CT appearance of the cranioventral mediastinum in the region of the thymus in supposedly normal adult dogs. Because of this variation, distinguishing residual thymic tissue from cranial mediastinal pathology may be difficult. For instance, small amounts of thymic tissue within the mediastinal fat may mimic hemorrhage or fat stranding due to inflammation, while more solid thymic tissue can be misinterpreted as a mediastinal mass. Because CT is a commonly used modality to evaluate the cranial mediastinum in dogs, knowledge of the range of normal features of residual thymic tissue in CT is important to avoid misdiagnosis and unnecessary interventions.[2]

The thymus is a lobulated organ originating from the third pharyngeal pouch. Because of its role in the development and maintenance of the immune system, it is of vital importance to the young animal.[3] The thymus is located in the ventral aspect of the cranial mediastinum and is laterally bordered by the lungs. When fully developed in dogs, it is positioned dorsal to the sternum with its cranial pole extending several centimeters cranial to the first rib and the caudal pole extending approximately until the level of the 5th or 6th rib on the left side of the heart.[4,5] Microscopically, the thymus is incompletely divided into lobules by connective tissue septa. The parenchyma of each lobule consists of lymphocytes and is divided into a cortex and medulla. Typical structures that are found in the thymus are epithelial reticular cells and Hassall's corpuscles, which are concentric whorls of flattened reticular cells.[6] The thymus grows rapidly during the first postnatal months and undergoes involution starting around 6 months of age.[7] During involution, the lymphoid tissue is gradually replaced by fat, which in some individual animals continues throughout life.[3] In dogs it is described that microscopically, small islands of thymic cells may remain present in the cranioventral mediastinum even in old age.[4] In human medicine, the presence of thymic tissue is described as a normal finding in CT of the thorax in adults, with a good correlation between CT findings and histological results.[8–10] The residual thymic tissue appears as smooth to irregular soft tissue in the cranioventral mediastinum with variable size, shape, and attenuation depending on the extent of fatty involution.[8,10] Studies in humans demonstrate a positive correlation between the extent of fatty involution and age, body mass index, stress, and certain diseases such as neoplasia and viral infections.[8,9,11–14] Besides that, women show significantly higher attenuation of the thymic gland, corresponding to less fat infiltration.[14,15] A paper evaluating thymic immunocompetency in several dog breeds found a decreased thymic output in larger breeds at a younger age than in smaller breeds, and no difference in thymic output between dogs of different sex or neutering status. This suggests that thymic involution in dogs may be associated with age and breed, but not sex or neutering status.[16] In another study, infection with canine distemper virus was found to cause thymic hypotrophy in puppies.[17] A recent study by Cordella et al.[18] describes the CT characteristics of the thymus in eleven adult dogs diagnosed with neoplasia, suspected to have rebound thymic hyperplasia.

Based on our review of the literature however, no reports confirming the presence or describing the prevalence and CT features of residual thymic tissue in a large population of adult dogs were available. The objective of the current study was to investigate the prevalence and appearance of presumed residual thymic tissue in CT images of the thorax in adult dogs. Our first aim was to compare CT findings in the cranioventral mediastinum with histological findings in a small group of patients to confirm the presence or absence of residual thymic tissue. The second set of aims was to describe the CT prevalence and appearance of presumed residual thymic tissue in a large group of adult dogs and to investigate any correlation between age and sex. The authors hypothesized that presumed thymic tissue would be a common finding in adult dogs and that the CT characteristics would be highly variable and would differ among dog signalment groups.

2 | METHODS

2.1 | Selection and description of subjects

2.1.1 | Part 1 prospective study

This was a prospective, descriptive design. A convenience sample of cadaver dogs meeting the following inclusion criteria was recruited at the Utrecht University Faculty of Veterinary Medicine hospital (Utrecht, The Netherlands) during the period of June 2021 to August 2022: deceased adult dogs of >1 year old (after sexual maturity) that died of causes presumed to be unrelated to thoracic disease. The animals died a natural death or were humanely euthanized. Decisions for subject inclusion were made by a second-year European College of Veterinary Diagnostic Imaging (ECVDI) resident (S.C.V.). Institutional animal care and use committee approval was not required because only cadaver dogs were used. Animal owners provided informed consent by signing a general patient consent form.

2.1.2 | Part 2 retrospective study

This was a retrospective, analytical design. Institutional animal care and use committee approval was not required because of the retrospective nature of the study. The hospital director approved the use of the patient data for this study. The Picture Archiving and Communications System (PACS) was reviewed for cases presented during the period of January 2020 to January 2021 at the Utrecht University Faculty of Veterinary Medicine hospital (Utrecht, The Netherlands) and that met the following inclusion criteria: thoracic CT studies of adult dogs (>1 year of age). If the same dog underwent multiple studies, the most recent study was used. Cases with the following characteristics were excluded: cranial mediastinal pathology, pleural effusion, poor image quality, and presence of soft tissue attenuation that could either represent lymph node tissue or thymic tissue, resulting in doubt about the presence and/or morphology of residual thymic tissue. Final decisions for inclusion or exclusion were made by a second-year ECVDI resident (S.C.V.) and an ECVDI-certified veterinary radiologist (I.A.S.).

2.2 | Data recording and analysis

2.2.1 | Part 1 prospective study

A thoracic CT scan was performed within 24 hours after death using a 64-multislice CT scanner (SOMATOM Definition AS, Escel Edition, Siemens AG). The images were evaluated by a second-year ECVDI resident (S.C.V.) at a PACS workstation using image analysis software

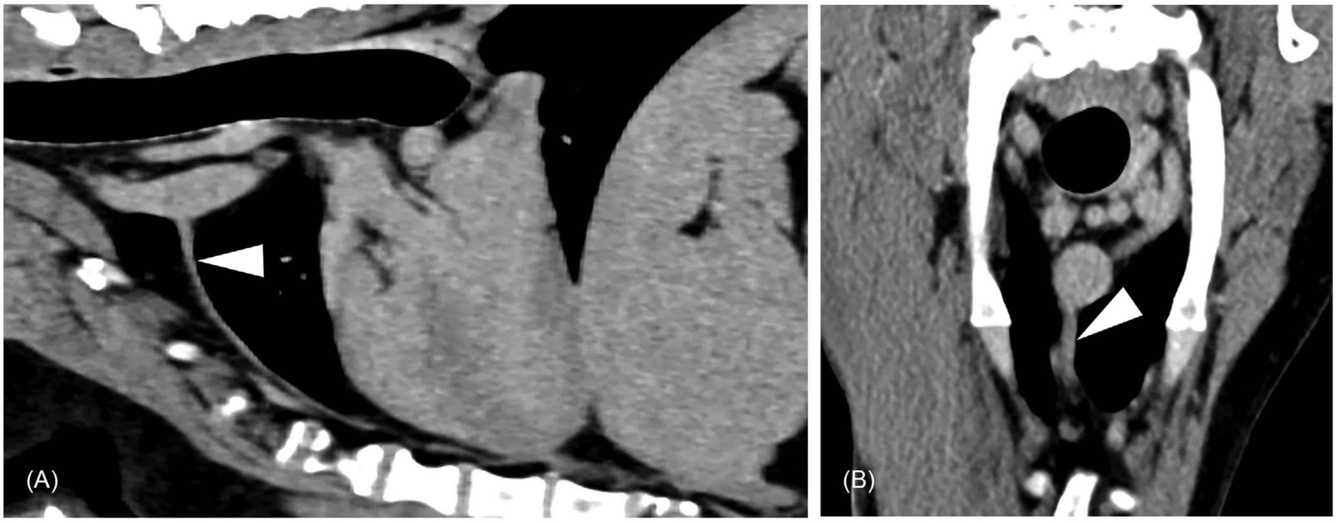

FIGURE 1 Sagittal (A) and transverse (B) postcontrast CT images of the cranial thorax of a 9.4 years old Labrador Retriever mix without visible presumed residual thymic tissue in the cranioventral mediastinum. The arrowheads indicate the internal thoracic veins before insertion into the cranial vena cava, which is used as a landmark to divide the cranioventral mediastinum in the cranial and caudal compartment in this study. Helical scan, 120 kVp, 65–185 mAs, slice thickness of 2 mm, pitch of 0.9, 512 × 512 matrix. Right (A) and cranial (B) are on the left side of the image.

(Enterprise Imaging, Agfa HealthCare N.V., version 8.1.2). Transverse images in soft tissue kernel were assessed for the presence of soft tissue attenuation in the cranioventral mediastinum other than lymph nodes or blood vessels. The following patient data were recorded: breed, age, sex, and cause of death. The CT images were subjectively evaluated for the presence of presumed residual thymic tissue in the cranioventral mediastinum, while the observer was not blinded to the signalment and clinical history. The location of the tissue was categorized as cranial (thoracic inlet extending to the internal thoracic veins, before the insertion into the cranial vena cava), caudal (internal thoracic veins to the heart), or both cranial and caudal (thoracic inlet to the heart; Figure 1). Cases where the presumed thymic tissue continued caudally on the left side of the heart were recorded. The shape of the thymus in the transverse plane was subjectively classified as flat, triangular, rounded, lobulated, or irregular. It was recorded if the presumed residual thymic tissue was interrupted and therefore consisted of more than one soft tissue attenuating area instead of being continuous. The attenuation was classified as homogeneous, heterogeneous (combination of soft tissue attenuation and fat), or mixed. Presumed residual thymic tissue was categorized as mixed when both areas of homogeneous and heterogeneous attenuation were present. This tissue of interest was then sampled after macroscopic assessment by a European College of Veterinary Pathologists (ECVP)-certified pathologist (W.B.), within 4 days after death. Subsequently, the tissue was fixed in 10% neutral-buffered formalin, routinely processed, stained with hematoxylin/eosin, and evaluated by light microscopy. If necessary, immunohistochemistry for keratin to confirm the presence of epithelial cells was performed. The histology results were compared with the findings in the CT images.

2.2.2 | Part 2 retrospective study

The CT studies were performed using the same CT scanner as used for the cases in the prospective study. A second-year ECVDI resident (S.C.V.) and an ECVDI-certified veterinary radiologist (I.A.S.) reviewed all images in DICOM format at a PACS workstation using the same image analysis software as used for the prospective cases, while the observers were not blinded to the signalment and clinical history. Both pre- and postcontrast (Iobitrodol, Xenetix 350 mg I/ml, Guerbet; 2 mL/kg injected in the cephalic vein using a power injector at 2 mL/s, up to a maximum of 60 mL/dog, delay time of 60 s after initiation of contrast administration) images (when available) were assessed. Reconstructions in the transverse plane, with adjustable window width and level and using a soft tissue and bone kernel, were used and decisions were based on consensus opinions. Dorsal and sagittal image reconstructions were used to verify thymus borders if necessary. The following patient data were recorded: breed, age, sex, and imaging diagnosis. Like the prospective study, the CT images were subjectively evaluated for the presence of presumed residual thymic tissue in the cranioventral mediastinum, and the location, shape, and attenuation were likewise recorded. Additionally, Hounsfield unit (HU) measurements were performed to provide objective attenuation observations in both pre- and postcontrast images (when available) using a circular region of interest (ROI) of maximum possible diameter on the slice at the widest part of the tissue in the transverse plane. Finally, the maximum width of the presumed thymic tissue was recorded in the same slice, followed by the measurement of the width of the proximal third of the rib closest to this slice (using the bone kernel). From these data, the thymus:rib ratio was calculated.

TABLE 1 Computed tomographic findings of six necropsy cases in the prospective part of the study.

Necropsy result	Thymic tissue (confirmed or suspected) (*n* = 5)	Hemorrhage (*n* = 1)
Location in cranioventral mediastinum (*n*)	Caudal: 2 (40%) Cranial + caudal: 3 (60%)	Cranial + caudal
Left lateral to the heart (*n*)	Yes: 1 (20%) No: 4 (80%)	No
Shape (*n*)	Mixed: 2 (40%) Flattened: 1 (20%) Irregular: 2 (40%)	Irregular[a]
Interrupted (*n*)	No: 5 (100%)	Yes[b]
Attenuation (*n*)	Homogeneous: 1 (20%) Heterogeneous: 3 (60%) Mixed: 1 (20%)	Heterogeneous

[a]Irregular soft tissue attenuation in the cranial mediastinum that appeared as ill-defined wispy to streak-like areas.
[b]The soft tissue attenuation in the cranioventral mediastinum consisted of multiple areas.

2.3 | Statistics

Data from the retrospective study were analyzed by a second-year ECVDI resident (S.C.V) under the supervision of a board-eligible ECVDI resident (D.H.N.B) using statistical software (IBM SPSS Statistics, version 28.0). The distribution of numerical variables was assessed for normality by the Shapiro–Wilk test and visual inspection of quantile–quantile plots. Because the assumption of Gaussian distribution of the data was not met, nonparametric testing was used and continuous data are presented as median (range). Dogs were classified into groups for analyses based on the following criteria: sex, presence of presumed thymic tissue, and attenuation of the tissue. Groups were compared using the Mann–Whitney *U* test (two groups) or the Krusal–Wallis test followed by Dunn's post hoc comparison (≥3 groups). Proportions among groups were compared using Fisher's Exact Test. Spearman's rho test was used to investigate any association between age and thymus:rib ratio. For the evaluation of significance in all tests, the *P*-value was set at <.05.

3 | RESULTS

3.1 | Part 1 prospective study

The convenience sample consisted of six deceased dogs that underwent postmortem CT followed by necropsy. There were three male neutered dogs, two male intact dogs, and one female neutered dog. The following breeds were represented: Beauceron, Border Collie, Boomer, crossbreed dog, Jack Russel Terrier, and French Bulldog. The median age of the dogs was 10.6 (5.4—14.4) years. Five dogs were euthanized because of various reasons presumed to be unrelated to thoracic disease: sepsis, shock, geriatric vestibular syndrome, liver failure, and paraparesis. One dog (Jack Russel Terrier) died naturally of a hemoperitoneum due to a ruptured hemangiosarcoma. The CT scans were performed using a standardized thorax protocol (helical scan, 120 kVp, 65–185 mAs, slice thickness of 2 mm, pitch of 0.9, 512 × 512 matrix) in lateral, dorsal, or sternal recumbency. The necropsy results and concurrent CT findings are listed in Table 1. Figure 2 shows transverse CT images of the cranial mediastinum of all six dogs: Beauceron in 2A, Border Collie in 2B, Boomer in 2C, crossbreed dog in 2D, Jack Russel Terrier in 2E, and French Bulldog in 2F. Five dogs showed soft tissue attenuation in the cranioventral mediastinum other than lymph nodes or vasculature, which was presumed to be residual thymic tissue. One dog (French Bulldog, male intact of 6.6 years that was euthanized because of shock) showed soft tissue attenuation in the cranioventral mediastinum as well, but with different morphologic characteristics: widening of the cranial mediastinum with multiple ill-defined, irregular, wispy to streak-like soft tissue attenuating areas diffusely distributed in the cranial mediastinum (Figure 2F). Because of this atypical presentation, pathology of the cranial mediastinum was suspected in this dog. Macroscopically, tissue consistent with the thymus was visible in two dogs. In three dogs only fat tissue was visible at the site of interest. The dog with the atypical presentation of soft tissue attenuation in CT showed extensive hemorrhage in the cranial mediastinum. Microscopically, the first five dogs showed areas of lymphoid tissue without differentiation between cortex or medulla, surrounded by well-differentiated fat tissue. In three of these dogs, groups of epithelial cells or Hassall's corpuscles were visible between the lymphoid tissue, and in one dog presence of epithelial cells could be confirmed with an immunohistochemical keratin stain. Therefore, the presence of involuted thymic tissue could be confirmed in these four dogs. In one dog (Jack Russel Terrier), no epithelial cells could be demonstrated and therefore the presence of thymic tissue could not be confirmed. As the present tissue was however of lymphoid origin, but not consistent with lymph node, the presence of thymic tissue in this dog is likely. Additionally, multifocal cyst-like structures surrounded by 1 to 2 layers of cuboidal to flattened epithelial cells, some ciliated, and filled with eosinophilic material were present in the sampled tissue of the previously described five dogs, most likely representing multiple small ultimobranchial cysts. In one dog, multiple macrophages with brown granular pigment were also detected, consistent with siderophages, suggesting previous hemorrhage. The dog with macroscopic

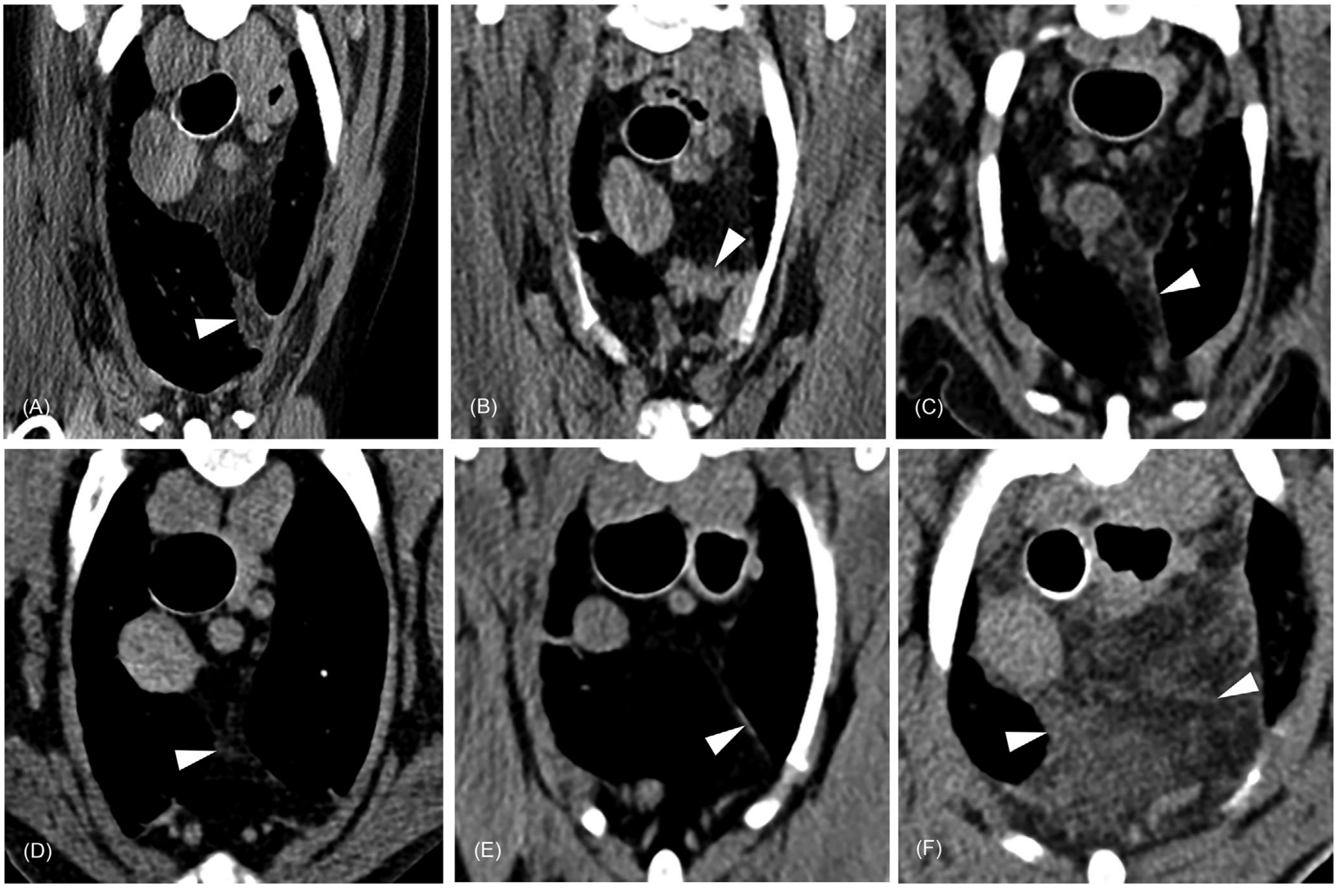

FIGURE 2 Transverse CT image of the cranial thorax (caudal to the internal thoracic veins and cranial to the heart) of six deceased adult dogs: a Beauceron (A), Border Collie (B), Boomer (C), crossbreed dog (D), Jack Russel Terrier (E), and French Bulldog (F). These images show different presentations of soft tissue attenuation in the cranioventral mediastinum (white arrowheads) histologically confirmed as residual thymic tissue in images (A)–(D), lymphoid tissue likely to represent residual thymic tissue in (E) and mediastinal hemorrhage in image (F). (A, C, and D) Irregularly shaped heterogeneous soft tissue attenuation in the cranioventral mediastinum. (B) Irregularly shaped homogeneous soft tissue attenuation in the cranioventral mediastinum. (E) A small amount of flattened, homogeneous soft tissue attenuation in the cranioventral mediastinum. The cranial aspect of this tissue (not included in the image) was heterogeneous in attenuation and it was therefore categorized as mixed. Note the atypical presentation with widening of the cranial mediastinum and multiple ill-defined, wispy to streak-like soft tissue attenuating areas in the cranial mediastinum (white arrowheads) in (F). Helical scan, 120 kVp, 65–185 mAs, slice thickness of 2 mm, pitch of 0.9, 512 × 512 matrix. The right is on the left side of the images.

mediastinal hemorrhage showed a marked amount of blood on histology, which hindered the evaluation for the presence of thymic tissue.

3.2 | Part 2 retrospective study

A total of 221 adult canine thoracic CT studies were retrieved. After applying the exclusion criteria, 52 cases were eliminated: soft tissue attenuation that could either represent lymph node tissue or thymic tissue, resulting in doubt about the presence and/or morphology of residual thymic tissue (presenting as irregular or nodular soft tissue structures; $n = 39$) (Figure 3), cranial mediastinal pathology (hemorrhage: $n = 3$; cranial mediastinal mass: $n = 2$; suspected mediastinitis: $n = 1$; mediastinal cyst: $n = 1$), pleural effusion ($n = 4$) and poor image quality ($n = 2$). Of the 169 dogs included in the study, 78 (46.2%) were female and 91 (53.8%) were male. This was further divided into eighteen (10.7%) female intact, 36 (21.3%) male intact, 60 (35.5%) female spayed, and 55 (32.5%) male neutered dogs. The median age was 9.2 years (range, 1.2–14.3 years) and a wide range of both small and large breeds were represented, with most commonly included: crossbreed dog ($n = 31$), Labrador Retriever ($n = 13$), Belgian Malinois (n = 6), Golden retriever (n = 6), Beagle (n = 5), and French Bulldog (n = 5). The CT studies were performed using the same CT protocol as used for the cases in the prospective study and transverse bone kernel images with a slice thickness of 0.6 mm were added for complete assessment. A total number of 87 precontrast and 122 postcontrast studies were available (both pre- and postcontrast studies were available in 48 dogs). Except for the pre- or postcontrast images in 113/161 dogs, there were no missing data. Presumed residual thymic tissue was observed in the cranioventral mediastinum in 161 (95.3%) of the dogs. Of the eight dogs without detectable thymic tissue, five dogs were

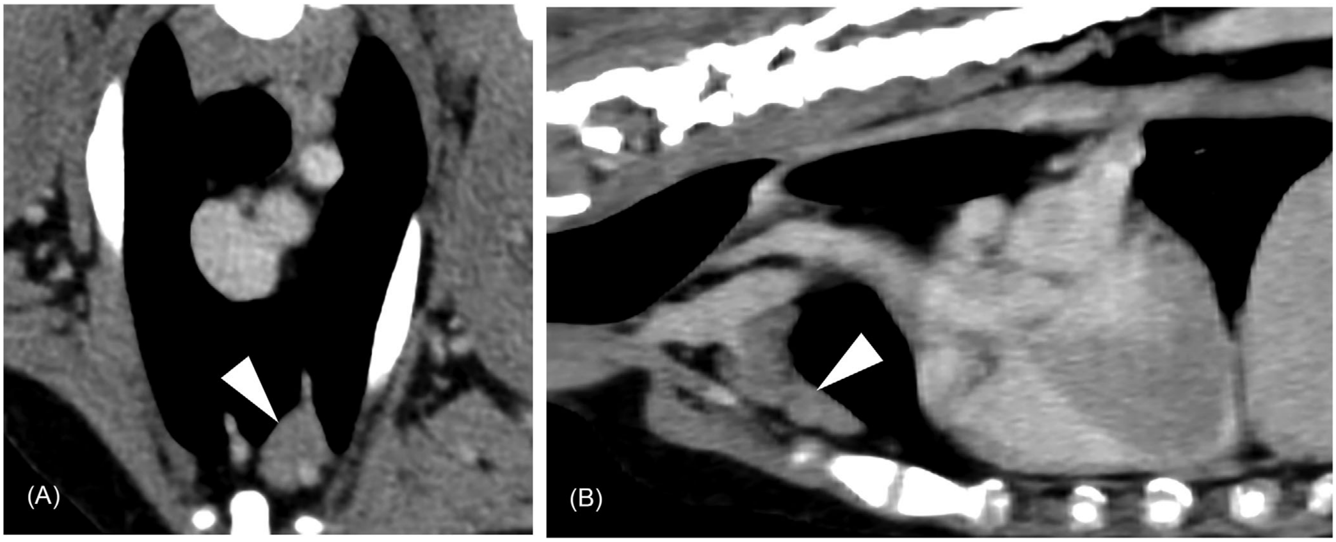

FIGURE 3 Transverse (A) and parasagittal (B) postcontrast CT images of the cranial thorax of 12.4 years old Lagotto Romagnolo with an aggressive lesion in the maxilla, showing a well-defined, homogeneous, lobulated soft tissue attenuating structure on the left side in the cranioventral mediastinum dorsal to the first and second sternebra (white arrowheads). No clear distinction between thymic tissue or sternal lymph node could be made, resulting in exclusion of this patient from the study. Helical scan, 120 kVp, 65–185 mAs, slice thickness of 2 mm, pitch of 0.9, 512 × 512 matrix. Right (A) and cranial (B) is on the left side of the image.

shepherds: Belgian Malinois (n = 2), Dutch Shepherd (n = 1), German Shepherd (n = 1), and Anatolian Shepherd (n = 1). The remaining three dogs were a Jack Russel Terrier, a Yorkshire Terrier, and a large crossbreed dog. Results of the CT appearance of presumed residual thymic tissue are presented in Table 2. The tissue was present in the cranial, caudal, or both parts of the cranioventral mediastinum in 2/161 (1.2%), 70/161 (43.5%), and 89/161 (55.3%) dogs, respectively. In 25/161 (15.5%) dogs, the tissue continued on the left craniolateral aspect of the heart (Figure 4A). The shape of the presumed thymic tissue was of mixed categories in most dogs (57.1%). When one category was present, the flattened (16.1%) and triangular (11.8%) shape were most common. In 39/161 (24.2%) dogs, the tissue was interrupted and consisted of two soft tissue attenuating areas (Figure 4B). The attenuation was homogeneous in 75/161 (46.6%), heterogeneous in 69/161 (42.9%), and mixed in 17/161 (10.6%) dogs (Figure 4C and D). The median maximum width of the tissue was 8.4 mm (1.8–37.8) and of the ribs 6.4 mm (2.6–10.0), with a median calculated thymus:rib ratio of 1.53 (0.40–6.52). A statistically significant difference in age was found for the presence of presumed residual thymic tissue, with dogs with presumed thymic tissue being younger (median: 9.1 years; range: 1.2–14.3) than dogs without (median: 10.5 years; range: 9.4–12.3; P = .036). When investigating age differences between the three attenuation groups, dogs with homogeneous attenuation were significantly younger than dogs with heterogeneous attenuation of the presumed residual thymic tissue (median: 8.1 years; range: 1.2–14.3 and median: 9.5 years; range: 4.0–14.3, respectively; P = .021). No statistically significant association was found between the presence of presumed residual thymic tissue and sex, nor were there significant associations between attenuation and sex or age and thymus:rib ratio.

4 | DISCUSSION

Findings of this study supported our hypothesis that soft tissue attenuation in the cranioventral mediastinum in CT, presumed to be residual thymic tissue, would be a common finding in adult dogs (prevalence of 95.3%). The tissue showed marked variation in size, shape, and attenuation and was more common and homogeneous in attenuation in younger dogs. Findings that did not support our hypotheses were a lack of significant associations between the presence of presumed residual thymic tissue and sex, attenuation and sex, and age and thymus:rib ratio.

The study of Dixon et al.[10] found a good correlation between the CT findings and the histology results in humans. In the prospective part of the current study, histology of the cranioventral mediastinum was performed in six dogs, with confirmation of the presence of thymic tissue in four dogs and the suspected presence of thymic tissue in one dog. Because the CT characteristics of the dogs with histologically confirmed/suspected residual thymic tissue were similar to the dogs in the retrospective study, it appears likely for the retrospective mediastinal findings to reflect residual thymic tissue in most of the cases. The sample size of the prospective group was however small and may be insufficient to conclude that soft tissue attenuation in the cranioventral mediastinum will always represent thymic tissue. Therefore, the findings in the retrospective study are referred to as "presumed" residual thymic tissue. The dog with mediastinal hemorrhage showed different CT characteristics with widening of the cranial mediastinum and multiple irregular soft tissue attenuating areas, some with a wispy to streak-like appearance. Thirty-nine dogs (24.2%) in the retrospective study showed interruption of the presumed residual thymic tissue as well, but here the tissue was divided into maximum of two parts. Also,

TABLE 2 Computed tomographic appearance of residual thymic tissue of the retrospective study cases.

Morphologic characteristics	Variables	Results ($n = 161$)
Location in cranioventral mediastinum	Cranial	2 (1.2%)
	Caudal	70 (43.5%)
	Cranial + caudal	89 (55.3%)
Left lateral to heart	Yes	25 (15.5%)
	No	136 (84.5%)
Shape	Mixed	92 (57.1%)
	Flattened	26 (16.1 %)
	Triangular	19 (11.8%)
	Irregular	15 (9.0%)
	Lobulated	6 (3.7%)
	Rounded	3 (1.9%)
Interrupted	Yes	39 (24.2%)
	No	122 (75.8%)
Attenuation	Homogeneous	75 (46.6%)
	Heterogeneous	69 (42.9%)
	Mixed	17 (10.6%)
Median Hounsfield Units (range)	Precontrast ($n = 78$)	9.4 (−99.3 to 72.8)
	Postcontrast ($n = 122$)	23.3 (−67.8 to 1003.0)
Median width (range)	Thymus (mm)	8.4 (1.8–37.8)
	Rib (mm)	6.4 (2.6–10.0)
	Thymus:rib ratio	1.53 (0.40–6.52)

a wispy to streak-like appearance or shape of the tissue was not seen in any of the dogs with presumed residual thymic tissue.

Besides residual thymic tissue and mediastinal hemorrhage, differential diagnoses for soft tissue attenuation in the cranial mediastinum include mediastinal effusion, mediastinitis, lymph node, cyst, hematoma, granuloma, abscess, neoplasia, thymic hematoma, and ectopic thyroid tissue.[19–23] In the retrospective part of the study, seven dogs were excluded after image evaluation because of suspected mediastinal hemorrhage, mediastinitis, mediastinal mass, or a cyst. Cranial mediastinal lymph nodes are described to vary in shape and number and most of them are located surrounding the large vessels of the cranial mediastinum.[4,24] The sternal lymph nodes are located immediately dorsal to the second or third sternebra, along the internal thoracic vessels. Usually, there is a single node on each side, but there may be fewer or more nodes on either side.[4,24,25] Using these described features, the observers are of the opinion that in most cases in the retrospective study, the distinction between presumed thymic tissue and lymph nodes was clear. In 39 cases, however, soft tissue structures were present in the cranioventral mediastinum that were not clearly categorized as either presumed residual thymic tissue or lymph nodes. Most of the time these structures were rounded nodules that were localized anywhere in the mid- to ventral part of the cranial mediastinum, from the thoracic inlet extending to the cardiac silhouette. To avoid misdiagnosis, these cases were excluded from the study as well. Ectopic thyroid tissue can be located anywhere from the tongue to the base of the heart, including the cranial mediastinum.[4,20,26–28] The prevalence of ectopic thyroid tissue is not described in dogs, but in humans, this is very low (0.9% with only 17.9% being mediastinal).[29] Ectopic thyroid neoplasia in dogs is most commonly seen in the area of the tongue or base of the heart and only a few reports of mediastinal ectopic thyroid neoplasia are available, which suggests that the presence of ectopic thyroid tissue in the cranial mediastinum is uncommon in dogs as well.[20,21,26–28,30] Taeymans et al.[31] describe the CT features of the canine thyroid gland and found pre- and postcontrast attenuation value ranges of 87.4–137.0 and 124.8–230.4, respectively. Although the high maximum HU value in the postcontrast images is suggestive of a measurement error (possible inclusion of a vessel in the ROI), attenuation values of presumed residual thymic tissue found in this study overlap with the findings of Taeymans et al.[31] This study, however, described the CT features of the normal thyroid gland, which may not be applicable to ectopic thyroid tissue. To summarize, distinguishing normal thymic tissue from ectopic thyroid tissue, lymph nodes or cranial mediastinal pathology may be challenging in some cases. However, because these tissues show different CT characteristics and/or low prevalence, it appears likely that the soft tissue attenuation described in the retrospective part of the study reflects residual thymic tissue in most of the cases.

In humans, fatty infiltration and therefore thymic involution progresses with age.[8,9,11,14] The study of Holder et al.[16] found that the same conclusions can be drawn for dogs, as age-associated reduction

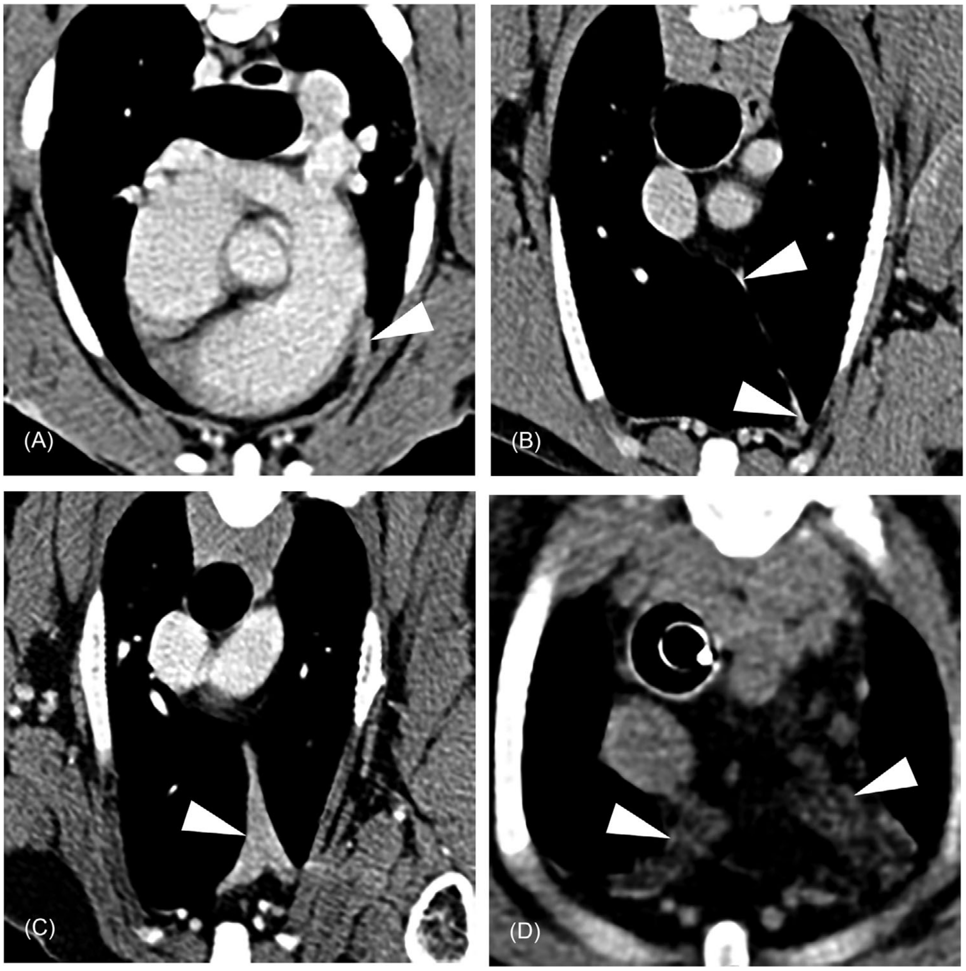

FIGURE 4 Transverse post- (A–C) and precontrast (D) CT images of the cranial thorax of dogs of different breeds and ages as examples of different morphologic appearances of presumed thymic tissue in the cranioventral mediastinum. (A) Presumed thymic tissue continuing on the left side of the heart (white arrowhead). (B) Interrupted presumed thymic tissue (white arrowheads). (C and D) Two different shapes and attenuations of the tissue: triangular and homogeneous (C) versus irregular and heterogeneous (D) (white arrowheads). Helical scan, 120 kVp, 65–185 mAs, slice thickness of 2 mm, pitch of 0.9, 512 × 512 matrix. Right is on the left side of the images.

in thymic output was seen. Also, large breeds with a relatively short life expectancy showed an earlier onset of decline in thymic output than smaller long-lived breeds, suggesting that thymic involution may occur earlier in the former breeds. In the current study, dogs with homogeneously attenuating presumed residual thymic tissue were significantly younger, and dogs without detectable presumed residual thymic tissue were significantly older, which is consistent with the previously described age-related thymic involution. The oldest dog included in this study, however, was 14.3 years old and this dog did show presumed residual thymic tissue on the CT images. In humans, Simanovsky et al.[9] found that after a certain age (54 years), no thymic tissue could be visualized in CT images.[9] Our results show that residual thymic tissue may be more common in younger dogs, but can remain visible in CT images in adult dogs, even in old age.

A wide range in width of the presumed residual thymic tissue, ribs, and thymus:rib ratio was found (1.8—37.8 mm, 2.6—10.0 mm and 0.40—6.52, respectively). The thymus:rib ratio was introduced to compensate for the size of the different dogs included in the study, but body conformation and body condition score were not taken into account. During the evaluation of the CT images, the authors noticed a large variation in the conformation of the thorax and mediastinum of different dog breeds. Brachycephalic breeds for instance are known for their barrel-shaped thorax and wide cranial mediastinum and dogs with a high body condition score show widening of the cranial mediastinum due to deposition of fat.[19] This may influence the appearance and width of residual thymic tissue in CT images. Therefore, the use of the thymus:rib ratio as a reference for the size of normal residual thymic tissue in adult dogs appears to be of limited value.

Five out of eight dogs without detectable residual thymic tissue in the CT images were shepherd dogs. Although the number of cases without detectable thymic tissue in CT was low, a predisposition for faster or more pronounced involution of the thymus may be suspected in these types of dogs. Holder et al.[16] describe breed-associated differences in thymic output related to age, although breeds in this study were categorized according to longevity and Shepherd dogs were not included.[16] As many factors are described to influence thymic fatty involution in both humans and dogs, it is plausible that breed differences can be seen in the CT appearance of residual thymic tissue in dogs.[8,9,11–17] Also, German Shepherd dogs are described to have larger spleens.[32] Although not previously described, the authors suggest this might be a result of redistribution of lymphoid functions from thymus to spleen. Future research is warranted, however, to examine if the presence and CT appearance of residual thymic tissue is related to certain breeds or body conformation.

For describing the location of the presumed residual thymic tissue in the cranioventral mediastinum, three categories were used: cranial (thoracic inlet to the internal thoracic veins), caudal (internal thoracic veins to the heart), or both cranial and caudal (thoracic inlet to the heart). Most dogs showed tissue in both the cranial and caudal (55.3%) or only the caudal (43%) compartment, with only 1.2% showing presumed residual thymic tissue in solely the cranial compartment. Although the location was not compared with age, this suggests that thymic involution in dogs starts cranially in the mediastinum. On the other hand, presumed residual thymic tissue was uncommonly seen at the left lateral aspect of the heart (15.5% of the cases), which is where the thymus caudally extends to in young dogs.[4] Comparing age with the location of presumed residual thymic tissue in the cranioventral mediastinum, possibly by dividing the cranial mediastinum into more categories, may provide more information on thymic involution in future studies.

This study has several limitations. As described earlier, the CT findings of the retrospective study were not histologically confirmed and therefore the presence of thymic tissue remains a presumption. Second, during the evaluation of the presumed residual thymic tissue in the CT image, recumbency of the patient was not taken into account. This may have influenced the appearance of the cranial mediastinum. Also, the observers were not blinded for the signalment and clinical history during evaluation of the CT images, and the CT characteristics were subjectively assessed. Although consensus opinions were used, knowledge of the age and diagnosis of the dogs may have influenced the assessment of the cranial mediastinum. To increase objectivity and repeatability, categories for the morphologic descriptions and measurements were used. Another limitation was the retrospective nature of the study and subsequent incomplete information on the clinical history and variation in CT protocol. Due to the retrospective selection of cases for the second part of the study, the study population consisted of dogs admitted to the hospital due to illness, which does not completely represent a normal population of (healthy) adult dogs. Also, the authors acknowledge that the absence of recorded clinical signs of thymic disease at the time of CT imaging does not exclude the possibility of subclinical disease.

In conclusion, findings indicated that, as in humans, presumed residual thymic tissue in the cranioventral mediastinum is a common incidental finding in CT images of the thorax of adult dogs. A wide variation in size, shape, and attenuation was seen in dogs with confirmed and presumed residual thymic tissue. Future larger cohort studies comparing CT findings of the cranioventral mediastinum with histological typing of the tissue present are, however, warranted.

LIST OF AUTHOR CONTRIBUTIONS

Category 1

(a) Conception and design: Vester, Bergmann, Veraa, Schaafsma
(b) Acquisition of data: Vester, Bergmann, Schaafsma
(c) Analysis and interpretation of data: Vester, Bergmann, Broek

Category 2

(a) Drafting the article: Vester
(b) Revising article for intellectual content: Bergmann, Broek, Veraa, Schaafsma

Category 3

a. Final approval of the completed article: Vester, Bergmann, Broek, Veraa, Schaafsma

Category 4

a. Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved: Vester, Bergmann, Broek, Veraa, Schaafsma

CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

PREVIOUS PRESENTATION DISCLOSURE

Preliminary results of the study were presented as a poster at the online EVDI conference, in September 2021.

REPORTING CHECKLIST DISCLOSURE

This study was reported according to STROBE guidelines.

DATA ACCESSIBILITY STATEMENT

Data are available from the corresponding author on reasonable request.

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