Short Communication

Computed tomographic assessment of vascular invasion and resectability of mediastinal masses in dogs and a cat

WE Scherrer[*§], AE Kyles[†], VF Samii[‡], EM Hardie[#], PH Kass[¥] and CR Gregory[¥]

Abstract

AIMS: To assess the sensitivity of non-angiographic contrast-enhanced computed tomography (CT) to determine the presence of vascular invasion of cranial mediastinal masses in dogs and a cat, and to evaluate the association between vascular invasion and peri-operative mortality.

METHODS: A retrospective study was conducted on 25 dogs and one cat. CT scans were completed with slices ranging from 2 to 10 mm. CT images were evaluated by a board-certified radiologist blinded to previous diagnoses and surgical findings. Each CT study was evaluated for vascular invasion, defined as disruption of the vessel wall and extension of the mass into the vessel lumen. Data retrieved from the surgery reports included surgical approach, whether vascular invasion was present, the surgeon's decision on operability, and post-operative complications.

RESULTS: Computed tomographic evaluation revealed 25/26 masses had no evidence of vascular invasion. During surgical exploration, 10/26 masses were found to invade major regional vasculature; the cranial vena cava (CVC) was the vessel most commonly invaded (7/10 animals), and 4/7 (57%) patients with invasion of the CVC were euthanised or died in the peri-operative period, from surgical or disease-related problems, which was significantly higher than patients without vascular invasion (p=0.045).

CONCLUSIONS: Non-angiographic contrast-enhanced CT was significantly less sensitive for detecting vascular invasion of cranial mediastinal masses when compared with surgical evaluation. If the CVC was invaded by a tumour there was a significant risk of death peri-operatively when compared with non-invasive cases.

CLINICAL RELEVANCE: Due to the significantly higher mortality risk associated with invasion of the CVC, a more sensitive method than CT should be investigated to determine vascular invasion of mediastinal masses pre-operatively.

KEY WORDS: *Computed tomography, mediastinal mass, thymoma, vascular invasion*

[*] Veterinary Surgical Associates, 907 Dell Ave, Campbell CA 95008, USA.
[†] NYC Veterinary Specialists, 410 W 55th Street, New York NY 10019, USA.
[‡] Ohio State University School of Veterinary Medicine, Department of Clinical Sciences, Columbus OH 43210, USA.
[#] North Carolina State University College of Veterinary Medicine, Department of Companion Animal and Special Species Medicine, Raleigh NC 27606, USA.
[¥] University of California Davis, School of Veterinary Medicine, Department of Surgical and Radiological Sciences, Davis CA 95616, USA.
[§] Author for correspondence. Email: bscherrer@vsasurgery.com

Introduction

Masses occurring in the cranial mediastinum are relatively frequently diagnosed in dogs and cats, the most common of which are thymoma and lymphoma (Carpenter and Holzworth 1982; Atwater *et al*. 1994; Mascort and Pumarola 1995). Occasionally, other mediastinal malignancies are diagnosed, such as neurogenic tumours, ectopic parathyroid and thyroid tumours, and heart-based tumours (Day 1997; Withrow 2007). Presently, the treatment of choice for most non-lymphoma cranial mediastinal masses in dogs and cats is surgical removal, with or without adjunct medical therapy. Thoracic imaging in these patients has traditionally involved radiography and ultrasonography. More advanced imaging modalities, such as CT and magnetic resonance imaging (MRI), have the potential to provide additional pre-operative information.

In human patients with mediastinal masses, CT has been shown to be superior to plain-film radiography for detecting, evaluating and staging these tumours (Rebner *et al*. 1987; Brown and Aughenbaugh 1991). The use of CT in veterinary medicine for the purpose of evaluating the characteristics of cranial mediastinal masses, such as contrast enhancement patterns, mass size, vascular invasion, lung metastasis, and lymphadenopathy has been documented. However, the ability of CT to predict whether a mass would be surgically resectable has not been evaluated (Yoon *et al*. 2004). Cranial mediastinal tumours can invade vascular structures, such as the aortic root, subclavian vessels, CVC, internal thoracic vessels, and axillary veins. The purpose of this study was to assess the sensitivity of contrast-enhanced CT to determine the presence and extent of vascular invasion of cranial mediastinal masses in dogs and a cat, to determine the feasibility of resecting cranial mediastinal masses which have invaded vascular structures, and to determine whether the presence of vascular invasion predicted peri-operative mortality.

Materials and methods

Medical records, thoracic radiographs, pre-operative CT studies and surgical reports from 25 dogs and one cat undergoing exploratory thoracotomy for treatment of cranial mediastinal masses between 1990 and 2003 were reviewed. CT scans were completed

CT	Computed tomography
CVC	Cranial vena cava
MRI	Magnetic resonance imaging
NCSU	North Carolina State University
OSU	Ohio State University
UCD	University of California Davis

with slices ranging from 2 to 10 mm, depending on the radiologist's preference. Contrast medium varied depending on the institution and date of administration; contrast media used included Iohexol 240 (Nycomed Inc, Princeton NJ, USA) at Ohio State University (OSU) and North Carolina State University (NCSU), and iothalamate meglumine 400 (Mallinckrodt Medical Inc, St Louis MO, USA) at the University of California Davis (UCD). Iohexol was given I/V immediately prior to scan initiation, at a dose of 0.45 ml/kg or 528 mg I/kg. Iothalamate meglumine was also given I/V immediately prior to scan initiation, at a dose of 0.45 ml/kg or 880 mg I/kg. CT scanners used were the Picker PQS helical scanner (Philips Medical Systems NA, Bethell WA, USA) at OSU, GE 9800 at UCD prior to 2001, GE HiSpeed FX/I helical scanner (General Electric Corp, Milwaukee WI, USA) at UCD from 2001 to 2003, and GE Sytec SR/I helical scanner (General Electric Corp) at NCSU.

Multiple data storage techniques were utilised to evaluate the thoracic CT scans, including DICOM and JPEG images read with efilm (Merge Healthcare, Milwaukee WI, USA). Eleven of the 26 cases were submitted from UCD using JPEG data, five were from OSU using JPEG data, and the other 10 from NCSU using DICOM data. All CT images were evaluated by one board-certified radiologist, who was blinded to previous diagnoses and surgical findings. Each CT study was evaluated for vascular invasion, defined as identification of contrast-filling defects in the vessel lumen, disruption of the adjacent vessel wall, and confluence of the intravascular filling defect with the extravascular mediastinal mass. If the mass was determined to be non-invasive, subjective assessment of vessel displacement by tumour contact or wrapping around regional vascular structures was noted. Data retrieved from the surgery reports included surgical approach, i.e. median sternotomy or lateral thoracotomy, whether vascular invasion was present, the surgeon's decision on operability, and post-operative complications. In patients with vascular invasion by tumour as determined subjectively by the surgeon intra-operatively, the vascular structures involved and the surgical techniques used were recorded. The peri-operative period was determined to be that time period the patient spent in the hospital, and ranged from 24 hours to 8 days. Peri-operative mortality was defined as death occurring prior to discharge from the hospital.

Statistical analysis

Findings from the surgery reports were correlated with CT evaluation by the board-certified radiologist. McNemar's χ^2 test was performed for pairwise comparison of CT and surgical evaluation of vascular invasion. Chi-squared tests of homogeneity were used to compare the distribution of the pathological diagnosis (thymoma, sarcoma, or fibrosarcoma) with outcome (alive or dead), invasion status (vascular invasion, no vascular invasion) with diagnostic imaging format (JPEG or DICOM), and outcome with diagnostic imaging format. The log-rank analysis was also used to determine significance in survival between patients with invasive *vs* non-invasive tumours. P-values <0.05 were considered statistically significant. Data were analysed using StatXact v7 (Cytel Software Corporation, Cambridge MA, USA).

Results

The mean (± SD) age at initial evaluation of the 25 dogs was 9.4 (SD 2.4) years. Of the dogs, two were entire males, 11 were castrated males, and 12 were spayed females. The feline patient was an 8-year-old castrated male.

Upon CT evaluation, 25/26 masses were non-invasive. Eleven masses were deemed non-invasive without evidence of displacement or wrapping around vascular structures. Seven were assessed as non-invasive but displacing local structures. One was interpreted to be non-invasive but wrapped around local structures. Six masses were considered non-invasive but displacing and wrapping around local vascular structures.

Surgical exploration revealed that the masses in 10/26 animals invaded major regional vasculature (Table 1). Most invasive masses involved more than one vascular structure. The CVC was the vessel most commonly invaded, followed by the internal thoracic vessels bilaterally, and bilateral invasion of the axillary veins in one. Of the three patients where invasion of the CVC was not documented, 2/3 of the surgical reports failed to specify which vessels were invaded, and in the other, the internal thoracic vessels were invaded bilaterally.

Of the 16 confirmed non-invasive masses six were submitted from UCD using JPEG images, four were submitted from OSU using JPEG images, and the remaining six were submitted from NCSU using DICOM images. Of the 10 invasive masses, five were submitted from UCD using JPEG images, one was submitted from OSU using JPEG image, and the other four were submitted from NCSU using DICOM images. The accurately predicted invasive tumour was submitted from NCSU using DICOM imaging; this mass did not involve the CVC. Of the seven masses which did invade the CVC, four were submitted from UCD and were read using JPEG images, one was submitted from OSU and was read using JPEG images, and the other two were submitted from NCSU and were DICOM images read using efilm. No significant relationship was found with regard to diagnostic imaging format and ability to predict invasion in general and invasion of the CVC in particular (p=1.00).

The surgical approach was a median sternotomy in 22/26 animals, a right intercostal approach in two, and a left intercostal approach in the other two. Surgical resection was attempted in 6/7 animals with invasion of the CVC. Surgical resection of masses invading the CVC required temporary partial or total occlusion of the CVC. The surgical techniques were resection of the mass and primary apposition of the CVC (n=4), or a technique described previously of venograft placement incorporating a portion of the jugular vein to stent the defect created after removal of a tumour thrombus from the CVC (n=1) (Holsworth *et al.* 2004). One animal with invasion of the CVC had the mass resected but the technique used was not recorded. Another patient with invasion of the CVC also had involvement of the axillary vein and phrenic nerve; the mass was deemed inoperable, and the patient was euthanised intra-operatively. With regard to the internal thoracic vessels, when resection of the mass was attempted, ligation of the internal thoracic vessels was the treatment employed for all patients. Overall, 3/10 masses with vascular invasion were deemed non-resectable by the faculty surgeon; one patient had an incisional biopsy of the mass performed and was discharged 5 days post-operatively, marginal debulking of the mass was attempted in one patient that died within 24 hours of the procedure, and the other patient was the one mentioned previously that was euthanised intra-operatively due to the nature of the mass.

In animals with vascular invasion, the pre-operative CT category was invasive in one animal, non-invasive in two, non-invasive

Table 1. Summary of computed tomographic (CT) evaluation, vessels invaded, surgical technique employed to remove the mass, and the patient's peri-operative outcome for nine dogs and one cat with invasive cranial mediastinal masses.

Case	University	CT evaluation (format)	Surgical evaluation	Surgical treatment	Peri-operative outcome
1	UCD	NI/D/W (JPEG)	CVC, bilateral internal thoracic arteries	Primary closure	Discharged 3 days post-operatively
2	UCD	NI/D/W (JPEG)	CVC	Primary closure	Euthanised 2 days post-operatively
3	UCD	NI (JPEG)	CVC	Jugular graft	Discharged 8 days post-operatively
4	UCD	NI/D (JPEG)	CVC, bilateral axillary veins	No resection attempted	Euthanised intra-operatively
5	UCD	NI (JPEG)	CVC	Primary closure	Euthanised within 24 hours post-operatively
6	OSU	NI/D/W (JPEG)	Vessels not specified	Incisional biopsy, no resection attempted	Discharged 5 days post-operatively
7	NCSU	NI/D (DICOM)	CVC, bilateral internal thoracic arteries	No description	Discharged 4 days post-operatively
8	NCSU	NI/D/W (DICOM)	CVC	Primary closure	Died within 24 hours post-operatively
9	NCSU	I/D (DICOM)	Bilateral internal thoracic arteries	Vessel ligation	Discharged 4 days post-operatively
10	NCSU	NI/D/W (DICOM)	Vessels not specified	Marginal resection	Died within 24 hours post-operatively

UCD = University of California Davis; OSU = Ohio State University; NCSU = North Carolina State University; NI = non-invasive; D = displacing regional vasculature; W = wrapping around regional vasculature; I = invasive; CVC = cranial vena cava

but displacing regional vasculature in two, and non-invasive but displacing and wrapping around regional vasculature in five animals. Hence, the sensitivity of CT to accurately predict vascular invasion was 10%. All 16 tumours found to be non-invasive at surgical exploration were accurately predicted by CT evaluation pre-operatively, yielding 100% specificity. When comparing the diagnosis of invasive *vs* non-invasive tumours, there was a significant difference between CT evaluation and surgical findings ($p=0.003$).

Fourteen of 16 patients with non-invasive cranial mediastinal masses were discharged from the hospital. Overall, 5/10 patients with invasive tumours died or were euthanised in the peri-operative period;. there was no significant difference when compared with the 2/16 patients that did not have invasive masses ($p=0.07$). In animals with invasion of the CVC, 4/7 patients were euthanised or died in the peri-operative period, from surgical or disease-related problems, e.g. respiratory arrest, hypotensive shock, or non-resectable tumour burden. Dogs with invasion of the CVC were more likely to die peri-operatively than those with non-invasive cranial mediastinal masses ($p=0.045$). Of the three animals with vascular invasion that did not involve the CVC, one animal died in the peri-operative period following attempted debulking.

Pathology reports were available for 25/26 patients. The cranial mediastinal mass was diagnosed as a thymoma in 16 animals; lymphoma in two; poorly differentiated sarcoma in two; and fibrosarcoma, neuroendocrine tumour, mesothelioma, histiocytic sarcoma, and basaloid carcinoma in one animal each. The animal which did not have histopathology performed was the patient with involvement of the CVC, axillary vein and phrenic nerve, which was euthanised intra-operatively.

Patients with vascular invasion had the following distribution. Of the 5/10 that died or were euthanised, 3/5 were diagnosed with thymomas, one had a sarcoma (feline), and one did not have pathology performed. Of the 5/10 that were discharged from the hospital, 3/5 were diagnosed with thymomas, one had a fibrosarcoma, and one had a sarcoma.

The feline patient was diagnosed by CT with a non-invasive mass that displaced and wrapped around the regional vasculature; the mass was found to invade the CVC at surgery. Resection of the mass and primary closure of the CVC defect was performed. This patient died in the peri-operative period, and the mass was diagnosed as a sarcoma. No significant relationship was identified with regard to pathology and survival ($p=1.00$).

Discussion

In the study presented here, contrast-enhanced CT was not sensitive for predicting vascular invasion of cranial mediastinal masses in pre-operative patients, as only 1/10 invasive tumours was accurately identified, and 0/7 tumours invading the CVC were accurately identified. This finding is similar to previous studies, which suggest that invasion of the CVC by the tumour may be the most serious interpretive challenge encountered when using CT for pre-operative staging in the dog and cat (Yoon *et al*. 2004). This apparent lack of sensitivity of CT for predicting vascular invasion of masses is not a problem unique to veterinary medicine. There is debate over the best diagnostic tool for evaluating and predicting vascular invasion of mediastinal masses in human patients. Studies comparing the use of MRI, positron emission tomography scan, CT scan, and combinations of diagnostic tools were unable to demonstrate a clearly superior imaging modality (Korobkin and Gasano 1989; Kubota *et al*. 1996; Yang *et al*. 1997; Pirronti *et al*. 2002). It was found that by utilising a grading scheme such as the one proposed by Lu *et al*. (1997), the sensitivity of CT for predicting vascular invasion of certain cancers in humans could be significantly increased. This uses a 0–4 grading system, where Grade-0 masses display no contiguity of tumour to vessel, Grade-1 masses are contiguous to <¼ circumference of the vessel (<90°), Grade-2 are 90–180° contiguous, Grade-3 are 180–270° contiguous, and Grade-4 have >270° of contiguity. Using this system, a predictive value for invasion of 89% was reported when tumours were graded as 2 or higher (Phoa *et al*. 2000; Brugel *et al*. 2004). To date, there is no similar grading scheme used in veterinary medicine to define vascular invasion of mediastinal tumours.

The presence of invasion of the CVC at surgery was an important and significant prognostic indicator. There was no significant difference in survival between patients with vascular invasion in general and those without vascular invasion. Additionally, it should be noted that the solitary feline patient presented in this study was diagnosed as having a non-invasive tumour by CT evaluation but at surgery was determined to have a mass invading the CVC. This patient died peri-operatively. However, it is not possible to draw conclusions for most cats based on the finding of this one patient.

As with any retrospective, multi-institutional study, there are multiple potential confounding variables. The lack of sensitivity in this study may have been in part due to the use of different formats for image analysis used in evaluating patients. As mentioned previously, 16/26 patients in total and 6/10 patients with invasive tumours had data submitted using JPEG images, significantly reducing the ability to alter or enhance image characteristics. Additionally, although one radiologist interpreted all of the images there were multiple CT scanners used at multiple institutions by various radiologists and technicians, allowing for multiple measurements and scanning techniques as well as subtle differences in administration of contrast medium. Further, as this was a retrospective study, complete data were not available for all animals.

In conclusion, the finding in this study of 10% sensitivity for CT imaging in predicting vascular invasion pre-operatively in dogs was substantially lower than anticipated. Furthermore, the high peri-operative mortality rate associated with invasion of the CVC would reveal a need to more accurately determine pre-operatively the invasive nature of cranial mediastinal masses, whether it is via a novel veterinary grading system, CT angiograms, or use of relatively new 3-dimensional reconstruction techniques offered by helical CT scanners, and imaging software allowing quantitative measurement of intraluminal Hounsfield units to help identify subtle intra-vascular filling defects. Precise pre-operative knowledge of the extent and vascular invasion of a tumour may not only aid in surgical planning, but equally importantly it will allow veterinarians to better inform owners prior to surgery.

References

Atwater SW, Powers BE, Park RD, Straw RC, Oglivie GK, Withrow SJ. Thymoma in dogs: 23 cases (1980–1991). *Journal of the American Veterinary Medical Association* 205, 1007–13, 1994

Brown LR, Aughenbaugh GL. Masses of the anterior mediastinum: CT and MRI imaging. *American Journal of Roentgenology* 157, 1171–80, 1991

Brugel M, Link TM, Rummeny EJ, Lange P, Theisen J, Dobritz M. Assessment of vascular invasion in pancreatic head cancer with multislice spiral CT: value of multiplanar reconstructions. *European Radiology* 14, 1188–95, 2004

Carpenter JL, Holzworth J. Thymoma in11 cats. *Journal of the American Veterinary Medicine Association* 181, 248–51, 1982

Day MJ. Review of thymic pathology in 30 cats and 36 dogs. *Journal of Small Animal Practice* 38, 393-403, 1997

Holsworth IG, Kyles AE, Bailiff NL, Hopper K, Long C, Ilkiw JE. Use of a jugular vein autograft for reconstruction of the cranial vena cava in a dog with invasive thymoma and cranial vena cava syndrome. *Journal of the American Veterinary Medical Association* 225, 1205–10, 2004

Korobkin M, Gasano VA. Intracaval and intracardiac extension of malignant thymoma: CT diagnosis. *Journal of Computer Assisted Tomography* 13, 348–50, 1989

Kubota K, Yamada S, Kondo T, Yamada K, Fukuda H, Fujiwara T, Ito M, Ido T. PET imaging of primary mediastinal tumours. *British Journal of Cancer* 73, 882–6, 1996

Lu DSK, Reber HA, Krasny RM, Kadell BM, Sayre J. Local staging of pancreatic cancer: criteria for unresectability of major vessels as revealed by pancreatic-phase, thin-section helical CT. *American Journal of Roentgenology* 168, 1439–43, 1997

Mascort J, Pumarola M. Posterior mediastinal paraganglioma involving the spinal cord of a dog. *Journal of Small Animal Practice* 36, 274–8, 1995

Phoa SS, Reeders JW, Stoker J, Rauws EA, Gouma DJ, Lameris JS. CT criteria for venous invasion in patients with pancreatic head carcinoma. *British Journal of Radiology* 73, 1159–64, 2000

Pirronti T, Rinaldi P, Batocchi AP, Evoli A, Di Schino C, Marano P. Thymic lesions and myasthenia gravis. Diagnosis based on mediastinal imaging and pathologic findings. *Acta Radiologica* 43, 380–4, 2002

Rebner M, Gross BH, Robertson JM, Pennes DR, Spizarny DL, Glazer GM. CT evaluation of mediastinal masses. *Computerized Radiolology* 11, 103–10, 1987

*__Withrow SJ.__ Thymoma. In: Withrow SJ, MacEwan EG (eds). *Small Animal Clinical Oncology*. 4th Edtn. Pp 795–6. WB Saunders Company, Philadelphia, USA, 2007

Yang WT, Lei KI, Metreweli C. Plain radiography and computed tomography of invasive thymomas: clinco-radiologic-pathologic correlation. *Australasian Radiology* 41, 118–24, 1997

Yoon J, Feeney D, Cronk D, Anderson K, Ziegler L. Computed tomographic evaluation of canine and feline mediastinal masses in 14 patients. *Veterinary Radiology and Ultrasound* 45, 542–6, 2004

Submitted 07 December 2007

Accepted for publication 01 July 2008

* Non-peer-reviewed