A descriptive review of cardiac tumours in dogs and cats


University of Liverpool, School of Veterinary Science, Small Animal Teaching Hospital, Neston, UK
*These authors have equally contributed to the review

Corresponding author: Elisabetta Treggiari, e.treggiari@gmail.com

Abstract

Cardiac tumours are uncommon in the canine and feline population and often an incidental finding. Common types include haemangiosarcoma (HSA), aortic body tumours (chemodectoma and paraganglioma) and lymphoma. These neoplasms can cause mild to severe, life-threatening clinical signs; they are independent of the histological type and may be related to altered cardiovascular function or local haemorrhage/effusion into the pericardial space.

Cardiac tumours may require symptomatic treatment aimed at controlling tumour bleeding and potential arrhythmias, and other signs caused by the mass effect. Other treatment options include surgery, chemotherapy and radiotherapy. For all medical therapies, complete remission is unlikely and medical management, beyond adjunctive chemotherapy in HSA, requires further investigation but combination chemotherapy is recommended for lymphoma.

The aim of this report is to summarize and critically appraise the current literature in a descriptive review. However, interpretation is limited by the lack of definitive diagnosis and retrospective nature of most studies.
Introduction

Cardiac tumours are uncommon in the canine population. Several small studies report an incidence between 0.12%\(^1\) and 4.33%\(^2\), while a larger retrospective study\(^3\) reported 1,383 dogs with tumours of the heart from a total population of 729,265 dogs (0.19% incidence) in a veterinary medical database. These neoplasms occur most frequently in middle age to older dogs, with the exception of lymphoma, which may also affect younger patients.\(^3\)

The aim of this report is to summarize and critically appraise the current literature in a descriptive review. However, interpretation is limited by the lack of definitive diagnosis and retrospective nature of most studies.

The most common type of cardiac tumour is haemangiosarcoma (HSA, 69\%).\(^3,4\) In addition to HSA, the following tumours are commonly reported: aortic body tumours (chemodectoma and paraganglioma)\(^4,5\), lymphoma\(^6\) and ectopic thyroid carcinoma.\(^3,4,7-9\) Less frequently, several other types of tumours are documented: thyroid adenoma\(^10\), melanoma\(^4\), mast cell tumour\(^4\), blastoma\(^4\), granular cell tumour\(^11\), mesothelioma\(^12-15\), myxoma\(^16-20\), myxosarcoma\(^21, 22\), mesenchymoma\(^23\), undifferentiated sarcoma of presumptive myofibroblastic origin\(^24\), fibroma\(^25\), fibrosarcoma\(^26-28\), rhabdomyoma\(^29\), rhabdomyosarcoma\(^30\), leiomyoma\(^31\), leiomyosarcoma\(^32\), chondrosarcoma\(^33, 34\), osteosarcoma\(^35-37\), paraganglioma\(^38\), peripheral sheath nerve tumour\(^39\), hamartoma\(^40\) and lipoma.\(^41-43\) Furthermore, single cases of valvular osteosarcoma\(^44\), valvular myxosarcoma\(^45\) and valvular metastasis of disseminated histiocytic sarcoma\(^46\) are described in the literature.

Cardiac tumours can be either benign or malignant (and primary or secondary).\(^7, 8\) Reports regarding the rate of primary versus secondary tumours in canine patients are contradictory: when retrospectively reviewing a veterinary medical database, Ware and Hopper reported that most of the tumours identified in the canine heart were primary (84\%) and only a 16\% were thought to be
metastatic.\textsuperscript{3,7} On the other hand, when Aupperle et al. reviewed necropsy findings with histological analysis, they reported cardiac tumours in 41% of the study population, and of these most were metastatic (69% metastases, 31% primary).\textsuperscript{7} In this study, metastases were found in the heart in 36% of the dogs with malignant neoplastic disease, which is comparable to humans where cardiac metastases are more common than primary cardiac tumours.\textsuperscript{7,47} The difference between the two veterinary studies likely reflects the different study populations: the Ware study\textsuperscript{3} cases were identified from a data base search for “cardiac tumours” and only two-thirds of the cases included had histological classification. Additionally, metastatic disease may have been coded in the database as the primary diagnosis, not as a cardiac tumour. In the necropsy study\textsuperscript{47}, clinically silent cardiac metastases are likely to have been identified, and in fact reports that cardiac metastases were not suspected based on clinical signs in any case.

A study assessing location of cardiac neoplasms documents that most primary cardiac tumours are located in the right atrium/right atrial appendage (63%), followed by heart base (18%) and left ventricle (9%).\textsuperscript{7} However, the data are derived mainly from post-mortem evaluations, thus possibly reflecting a bias towards the more aggressive or malignant types of cardiac tumours, including those that cause pericardial effusion or more severe clinical signs and patient death. Most right atrial/auricular masses, likely HSA, show malignant tumour characteristics including the tendency to metastasize, regardless whether they occur with or without pericardial effusion. In contrast, heart base masses such as chemodectomas often display more benign behaviour, with a low incidence of metastasis and variable occurrence of pericardial effusion; indeed some dogs may be completely asymptomatic. Thus tumours of this type are likely to be underestimated by post mortem-based studies. Other heart base tumours reported include adenomas and adenocarcinomas, with adenomas most common: these would similarly tend to be under-represented in a necropsy study.\textsuperscript{48,49}
Unlike primary tumours, most metastatic lesions reported by post-mortem (75%), are found in the inner third of the left ventricular free wall, in the interventricular septum, or both. Only 25% of metastatic tumours are found in the right atrium or right ventricular wall, or both.\textsuperscript{7, 50}

Ware et al. reported that the breeds with higher incidence of cardiac tumours are German Shepherd dogs (GSD), Golden Retrievers, Boxers, Bulldogs, Boston Terriers, Scottish terriers, English Setters, Afghan Hounds, Flat Coated retriever, Irish Water Spaniels, French Bulldogs and Salukis.\textsuperscript{3} Breeds specifically recognised to be at increased risk of developing cardiac HSA (as well as splenic HSA) are GSD and Golden Retrievers.\textsuperscript{3, 4} Brachycephalic dogs are predisposed to aortic body tumours, in particular Boxers\textsuperscript{4}; this was thought to be associated with chemoreceptors stimulation caused by chronic hypoxia\textsuperscript{51, 52}, however this hypothesis has never been proven and instead a genetic component is more likely.\textsuperscript{51} Secondary cardiac tumours can affect any breed.

**Most common canine tumour types**

**Haemangiosarcoma**

Haemangiosarcoma (HSA) is the most common cardiac tumour in dogs.\textsuperscript{3, 4} Diagnosis is often presumptive, and relies on imaging findings and anatomical location. HSA commonly presents as a mass involving the right atrium (Fig. 1C) and the right atrial appendage.\textsuperscript{3, 8} In the authors’ experience, HSA also infrequently presents as a diffuse infiltrative tumour (Fig.1D, Fig. 2B). Atrial HSA can present as a solitary tumour, or occur concurrently with a splenic mass.\textsuperscript{53, 54} The rate of concurrent right atrial masses in dogs that present to the veterinarian for investigations of splenic HSA varies between 8.7%\textsuperscript{53} and 25%\textsuperscript{54}, therefore echocardiography may be indicated in these cases as part of the staging process. On the other hand, the rate of concurrent splenic HSA in dogs that present to the hospital for cardiac HSA has been reported as 29%. Interestingly, 42% of these dogs
had non-splenic metastases at presentation\textsuperscript{53}: it is therefore unclear whether these patients have two primary tumours, or one primary and a metastatic lesion in the spleen. In addition, the risk for non-splenic metastasis appears to decrease with age, but an age related reduction in the frequency of concurrent splenic and cardiac HSA is not documented. Diagnosis is very rarely attempted by means of biopsy and/or cytology, because of the perceived risks of non-representative sampling and significant complications. Surgery and adjuvant chemotherapy have been described in the management of atrial HSA, with adjuvant chemotherapy being considered the most effective treatment in these cases.

**Lymphoma**

Lymphoma involving the heart and surrounding structures is infrequently reported in dogs. “Primary” cardiac lymphoma is defined in human medicine as lymphoma affecting the heart, the pericardium or both.\textsuperscript{55} According to the WHO criteria for staging of lymphoma in dogs, cardiac lymphoma with pericardial effusion is classified as stage V (extranodal in an organ other than liver or spleen), substage b (with clinical signs). This stage of lymphoma may be subject to a worse prognosis overall, but there is no specific data for the cardiac form. The largest study on cardiac lymphoma evaluated outcome in 12 dogs, of which 5 were treated with multidrug chemotherapy.\textsuperscript{6} In that report, cardiac lymphoma was diagnosed by means of cytology of the pericardial effusion in 8 dogs; immunohistochemistry was available for just 3 dogs, confirming T-cell origin in 2 patients and B-cell origin in one dog. Five dogs were treated with combination antineoplastic chemotherapy either after the initial therapeutic pericardiocentesis alone or after pericardiocentesis followed by partial pericardiectomy\textsuperscript{6}, but median survival times (MST) were short (157 days). One of the 5 dogs also received adjunctive radiation therapy. Seven dogs did not receive any treatment.
Aortic body tumours (chemodectoma/paraganglioma)

Aortic body tumours can potentially arise from any anatomical site, although chemodectomas seem to be the most common type, occurring in the wall of the ascending aorta at the level of the heart base. Chemodectomas are non-functional tumours of paraganglial cells and therefore believed to be essentially benign with low metastatic potential (Fig. 1 A-B, Fig. 2 A). Conversely, paragangliomas arise from paraganglial cells located within the atria along the root of the great vessels and derive from the visceral autonomic ganglia. Extra-adrenal paragangliomas that are functional and secrete catecholamines are usually chromaffin positive and have been termed chromaffin paragangliomas or non-adrenal pheochromocytomas. The current veterinary literature on this type of neoplasm is limited to case reports. A paraganglioma in an intracardiac location was identified at necropsy in the right atrium of a GSD which presented with signs of depression and anorexia. Successful surgical excision of a left atrial paraganglioma is described, resulting in a survival time (ST) of 2 years with no adjuvant treatment. A functional chromaffin paraganglioma in the right atrium was reported in a 5 year old Labrador that presented with ascites secondary to caudal vena cava obstruction: biopsies obtained through a left jugular venotomy were consistent with a neuroendocrine tumour, most likely chemodectoma. However, due to the dog’s clinical signs at the time of biopsies (transient hypertension and atrial fibrillation), a functional paraganglioma was suspected. This dog was euthanased hence no further outcome information was available, but electron microscopy showed numerous neurosecretory granules within the cytoplasm of the neoplastic cells, hence supporting the suspicion of a functional tumour. A similar report has described a case of a functional paraganglioma which stained positive for chromogranin indicating a neuroendocrine origin. Intracardiac metastases of an aortic body tumour have also been described in one dog, but metastases from these lesions seem uncommon.
Rhabdomyoma and rhabdomyosarcoma

The exact histogenesis of rhabdomyoma is uncertain, and whether cardiac rhabdomyoma is a true neoplasm or a hamartoma is still a controversial issue in the medical literature. In humans, cardiac rhabdomyomas are reported to regress spontaneously. Interestingly, a cardiac rhabdomyoma has been reported in a young Beagle (9 months-old), in which no signs of cardiac compromise were found; in this case the tumour was an incidental finding on necropsy and stained positive for PAS and desmin. The same tumour type has been reported in an older dog (6 years-old), associated with chylothorax.

Malignant muscle tumours are also described. A rhabdomyosarcoma was described in a GSD involving the right atrium and the right ventricle, causing right-sided heart failure (pleural, pericardial and abdominal effusions). The dog was euthanased after the mass was found on echocardiography and diagnosis confirmed at the time of necropsy. Another rhabdomyosarcoma was diagnosed in a Labrador Retriever with pericardial effusion, on biopsies obtained by thoracotomy. One case report in a Great Dane with a primary cardiac rhabdomyosarcoma, demonstrated involvement of the heart, lungs, diaphragm, liver, kidney and greater omentum, confirming that this tumour type has the potential to metastasise.

Clinical signs

Cardiac tumours can cause mild to severe, life-threatening clinical signs, or just be an incidental finding. The clinical signs caused by cardiac tumours are independent of the histological type and may be related to altered cardiovascular function caused by the mass effect or, more commonly, local haemorrhage/effusion into the pericardial space. Cardiac or pericardial tumours are responsible for most of the pericardial effusions documented in dogs (up to 60%), with HSA being the most common cause, followed by mesothelioma and aortic body tumours. Clinical signs associated with pericardial effusion secondary to cardiac neoplasia are not specific, but similar to
those caused by idiopathic pericardial effusion. Pericardial effusion can result in right atrial or even right ventricular tamponade and therefore cause decreased pre-load and compromised cardiac output and/or right-sided congestive heart failure.\textsuperscript{68} \textsuperscript{60,} \textsuperscript{61} Clinical signs may include acute collapse, exercise intolerance or lethargy and on physical examination there may be muffled heart sounds, tachycardia, pulse deficits, pale mucous membranes, weak femoral pulses, ascites, tachypnoea/dyspnoea or increased abdominal effort, subcutaneous oedema, jugular venous distension, jugular pulsations, positive hepatojugular reflux, weight loss and even vomiting.\textsuperscript{69,} \textsuperscript{70}

Dogs can also present with chylous effusions, either in the pleural\textsuperscript{9} or pericardial space.\textsuperscript{29}

Cranial vena cava syndrome can be observed in cases of heart base masses compressing the cranial vena cava. Syncopal episodes can also occur in cases of right ventricular outflow tract obstruction.\textsuperscript{71}

Occasionally, signs of left sided congestive heart failure can be present due to the location of the tumour, which can obstruct left ventricular inflow.\textsuperscript{3,} \textsuperscript{20} Sudden death is also reported, most likely related to rupture of the tumour with haemorrhage and/or cardiac tamponade, but also potentially secondary to arrhythmias.\textsuperscript{3} Tachyarrhythmias (mainly ventricular arrhythmias either due to the primary cardiac mass or associated with splenic/hepatic masses) or bradyarrhythmias (e.g. 3\textsuperscript{rd} degree atrio-ventricular block [AVB]\textsuperscript{31,} \textsuperscript{72}) have been described.

Aupperle \textit{et al.} reported that in dogs with metastatic cardiac tumours, the clinical presentation and symptoms correlated mainly with the primary extra-cardiac tumour: cardiac metastases were not suspected \textit{ante-mortem} in any case.\textsuperscript{50}

\textbf{Diagnosis}

History and physical examination may help in the diagnostic process, although cardiac tumours may produce no overt abnormalities on routine clinical examination, unless associated with pericardial effusion (as detailed above).

Cardiac masses can be difficult to detect and even after detection, obtaining a definitive diagnosis may be challenging. In the clinical setting, masses from extra-cardiac locations are routinely
sampled to achieve a cytological or histological diagnosis or as part of the staging of an oncologic condition. Whenever feasible, cardiac masses may also be aspirated as this will provide more prognostic information and allow specific treatment (Fig. 3). Sampling of cardiac masses is not a routine procedure, mainly given the potential risk of arrhythmias and haemorrhage. However, in the authors’ experience, this procedure is relatively safe and fine needle aspirates seem to have a reasonable diagnostic accuracy (unpublished data; manuscript under review). Transvenous endomyocardial biopsies and open chest or thoracoscopic biopsies can also be performed in selected patients and can provide a histopathological diagnosis (Fig. 4).

An electrocardiogram may be used as a diagnostic tool. Cardiac tumours can cause pericardial effusions and be associated with low voltage QRS and electrical alternans. In addition, conduction disturbances or arrhythmias (either tachy- or bradyarrhythmias) can also be detected. However, these findings are not specific for the presence of a cardiac neoplasm.

When pericardial effusion is present, cytology should be performed to try to distinguish benign from malignant pericardial effusions, or identify what type of cardiac neoplasia is present. A study evaluating the diagnostic utility of pericardial fluid analysis reported frequent false positive (13%) and false negative (74%) results. Its utility is variable depending on the tumour type, and there is an improved diagnostic yield from effusions with a PCV of less than 10%. MacGregor et al diagnosed cardiac lymphoma in 7/12 cases by means of pericardial fluid analysis, possibly because samples of lymphoid tumours are usually associated with a higher cellularity and more likely to be exfoliative and less haemorrhagic. The pH of the pericardial effusion has also been evaluated as a mean to distinguish between idiopathic or neoplastic effusion, however due to a significant overlap between the two groups, this is not currently recommended as a diagnostic test.

The utility of serum concentrations of Troponin I and Troponin T to diagnose cardiac neoplasia and to differentiate benign from malignant pericardial effusions has been investigated. Serum troponin I
was shown to be higher in dogs with cardiac HSA than in dogs with extra-cardiac HSA, dogs with extra-cardiac neoplasia other than HSA and dogs with pericardial effusion not caused by HSA.\textsuperscript{81, 82} In cases of pericardial effusion, Troponin I increases not only in the plasma but also in the pericardial fluid, but the concentration of Troponin I in the effusion does not appear to help differentiating between aetiologies.\textsuperscript{83} Troponin T was not significantly different between dogs with idiopathic pericardial effusion and dogs with pericardial effusion caused by a cardiac HSA.\textsuperscript{82}

Thoracic radiographs can raise the suspicion for cardiac tumours or pericardial effusion, if there is a visible change in the cardiac silhouette. For staging purposes, lung metastases can also be identified.\textsuperscript{8}

Echocardiography has been shown to have a high specificity (100\%) and sensitivity (82\%) for the detection and characterisation of masses in dogs with pericardial effusion.\textsuperscript{84} The location and size of the tumour may help predict the diagnosis\textsuperscript{84} (for example HSA appears to be more common in the right atrium/right atrial appendage), but a presumptive diagnosis based on the anatomical location is only moderately accurate\textsuperscript{84, 85}, with an accuracy ranging from 50\% to 78\% depending on the tumour type (Fig. 1). In addition, reports of valvular primary or secondary tumours\textsuperscript{44-46} highlight the fact that such lesions have been misdiagnosed as endocarditis by less experienced ultrasonographers, and therefore a neoplastic process should be considered as a differential diagnosis in some cases of valvular abnormalities.

Advanced imaging modalities such as computed tomography (CT), positron emission tomography (PET) scans (Fig. 5) and magnetic resonance imaging (MRI) are useful diagnostic tools for detection of cardiac tumours.\textsuperscript{67, 86-88} Pneumopericardiography\textsuperscript{47}, angiography\textsuperscript{71} and gated radionuclide imaging\textsuperscript{58} are also reported. Multidetector CT was not superior to echocardiography in
detecting cardiac masses in dogs with pericardial effusions despite its benefits in the identification of pulmonary metastases.\textsuperscript{89}

Cardiac MRI was used to differentiate neoplastic from non-neoplastic pericardial effusions, but this modality did not improve the accuracy of a final diagnosis of cardiac tumours when compared to echocardiography.\textsuperscript{90}

**Treatment and prognosis**

Multiple treatment options exist for cardiac tumours including surgery, chemotherapy and radiotherapy (RT), in addition to symptomatic treatment, which may be necessary to stabilise patients that present with cardiac tamponade (e.g. pericardiocentesis). Adequate control of the primary tumour is often difficult to achieve and this limits survival, particularly in cases with severe clinical signs. The lack of a definitive diagnosis in most cases may also mean that some patients do not receive the most appropriate treatment: this is most relevant if a chemosensitive tumour (e.g. lymphoma) is not diagnosed.

Without treatment, the prognosis for cardiac tumours is variable but generally poor. A study of 51 dogs diagnosed with histologically-confirmed HSA reported median survival times (MST) of 7.1 days (range, 1 to 26 days) for dogs that received no treatment.\textsuperscript{91} Pericardiocentesis as palliative monotherapy is also associated with a poor outcome.\textsuperscript{68, 84, 92-94}

**Surgery**

Pericardiectomy for dogs with cardiac tumour associated pericardial disease conveyed a MST of 52 days in 9 dogs\textsuperscript{92} compared to pericardiectomy for non-neoplastic pericardial disease (MST 792 days in 13 dogs).\textsuperscript{92} While this study only included a small number of dogs’ cases with confirmed cardiac neoplasia, it suggests that pericardiectomy is advantageous over just pericardiocentesis, given recurrence of clinical signs associated with pericardial effusion is one of the main causes of
death/euthanasia. Pericardiectomy does increase the potential risk of severe and acute haemorrhage into the pleural space (instead of a contained haemorrhage into the pericardial space), but overall appears to confer a survival advantage. Pericardiectomy and tumour resection resulted in a MST of 86 days (range 10-202 days) in a group of 12 dogs\textsuperscript{91}; in this case ST was found to be significantly longer when compared to dogs that received no treatment (8) or medical management alone (26). However, in another study on 143 dogs\textsuperscript{68}, MST and recurrence of pericardial effusion did not seem to be affected by pericardiectomy in dogs with cardiac HSA. However, these results have to be interpreted with caution, as the tumour diagnosis was only presumptive in the majority of cases included in that study.

Surgical excision is the treatment of choice for HSA, and is desirable as long as anatomic location permits (Fig. 6). There are a number of case series reporting successful surgery of cardiac tumours, though morbidity and mortality are high.

In a study on 51 dogs using traditional thoracotomy for HSA resection,\textsuperscript{91} MST was 86 days (range, 10 to 202 days) for dogs that had pericardiectomy and surgical resection of the HSA only and 189 days (range, 118 to 241 days) for dogs that had surgical excision of the HSA and adjuvant chemotherapy. This compares favourably to palliative pericardiocentesis with no additional treatment (MST 7.1 days, range 1 to 26 days) or with non-chemotherapeutic medical management only (MST 27 days, range 1 to 188 days\textsuperscript{91}). However, another study of 23 dogs\textsuperscript{94} reports shorter MST post surgery: MST was 42 days (range 0 to 138 days) for dogs treated with surgery alone, and 175 days (range 36 to 229 days) for the dogs treated with surgery and chemotherapy. In this study, pericardiectomy was also performed in 21 (91%) dogs, while the pericardium was closed in 2 (9%) dogs. The 2 dogs in that study in which the pericardium was closed did not receive chemotherapy and lived 23 and 138 days after surgery. In both studies, ST was significantly longer for dogs that received adjuvant chemotherapy after surgery compared to those who received surgery alone, however the role of adjuvant chemotherapy cannot be further clarified due to the retrospective
nature (and potential bias in advising treatment and timing of euthanasia due to owners’ decisions) of the study.

Thoracoscopic resection has been described in nine cases. Eight HSA and 1 pyogranulomatous lesion were resected, mainly from the right atrial appendage (8 dogs). One dog with a mass located at the base of the right auricle died during surgery, but no other postoperative complications were noted in the remainder of the patients. However, masses close to the base of the right atrial appendage may not be amenable to resection with thoracoscopy. Another report describes successful removal of a high right atrial HSA via subtotal thoracoscopic pericardiectomy, achieving a ST of 177 days in combination with chemotherapy.

There is a single case report describing a pericardial patch graft to repair the defect after resection of a right atrial HSA; this dog also received adjunctive carboplatin and recurrence was documented 7 months later. A palliative RT protocol was started at that point and ST was 260 days after diagnosis.

Aortic body and heart base masses that are not locally invasive may be more amenable to surgery. Malignant heart base masses tend to invade local vessels or lymphatics, making resection difficult. For aortic body tumours, the recommended treatment includes pericardiectomy in order to better control clinical signs (e.g. pericardial effusion). In one case series of 25 heart base masses, mean ST for dogs that underwent pericardiectomy (661 ± 170 days) was significantly longer than mean ST for dogs that were treated medically (pericardiocentesis, diuretics or chemotherapy), achieving a survival of 129 ± 51 days. There was no final diagnosis for any of the dogs in this study.
Chemotherapy

Surgical excision of HSA is the treatment of choice, but when this is not feasible, chemotherapy options include cyclophosphamide-based chemotherapy, single agent anthracyclines, or anthracycline-based combination therapy, but data are limited and limited efficacy is expected in a gross disease setting. Conventional chemotherapy is most effective in the minimal residual disease setting, and for splenic HSA is used as post-operative adjunctive therapy to try to delay development of clinically significant metastatic disease. A doxorubicin-based combination protocol (VAC protocol\textsuperscript{98}) for HSA has been shown to result in a MST of 172 days although no control group was included in the study and historical controls were used for comparison. Three dogs had concurrent right atrial as well as splenic involvement in this study, and this protocol has not been specifically evaluated for dogs with confirmed primary cardiac HSA.

In cardiac HSA, chemotherapy may offer a survival advantage when compared to pericardiocentesis alone, but without the ability to achieve a compartmental excision of the primary tumour, as is achieved by splenectomy, the impact on survival will likely be less than as an adjunct in splenic HSA.

In 23 dogs with cardiac HSA treated surgically\textsuperscript{94} by means of pericardiectionomy and mass resection, mean ST after surgery without chemotherapy ranged between 43-46 days, whereas mean ST was 164 days for dogs that also received adjuvant chemotherapy. Only eight of the 23 dogs received chemotherapy and protocols were doxorubicin alone in three dogs (ST 12, 36 and 188 days), doxorubicin and cyclophosphamide in three dogs (ST 118, 162 and 228 days) and doxorubicin, cyclophosphamide, and vincristine in one dog (ST 205 days). The chemotherapy protocol for the remaining dog was not specified. Time to initiation of treatment, cycles received and stage also varied between groups (with 7 [28\%] dogs with documented metastatic disease at presentation). Thus the study lacks the power to demonstrate any difference between protocols. An individual case report in a dog receiving single agent doxorubicin after surgery reports similar survival time (177
Doxorubicin was also used in a study on presumptive cardiac HSA identified by echocardiography in 16 dogs, treated with chemotherapy alone. Histopathological diagnosis was performed after post-mortem examination in only 1 case, confirming HSA. These authors used doxorubicin either alone or in combination in a multi-agent protocol as already described in previous studies and achieved a MST of 139 days.

A recent larger study compared the outcome of 64 dogs with a presumptive diagnosis of cardiac HSA on echocardiography, treated with doxorubicin as a first line treatment, versus 76 untreated patients. Although median progression-free survival (PFS) and MST were of short duration (66 and 119 days respectively) in those dogs receiving chemotherapy, the authors found an improved survival when compared to the untreated group, whose MST was 12 days only. None of the dogs received pericardiocentesis or surgery before receiving chemotherapy, with the responders experiencing either complete response (CR) or stable disease (SD). Following the completion of the doxorubicin-based protocol, 1 dog was treated with vincristine and cyclophosphamide, whereas 20 dogs that showed no response to doxorubicin received rescue chemotherapies (including vincristine, cyclophosphamide and carboplatin). Eleven dogs within the responders’ group also received metronomic cyclophosphamide, but this did not seem to affect the outcome significantly. Interestingly, metastatic disease at diagnosis was detected more frequently in the group receiving chemotherapy and this may have biased the clinician’s advice and subsequently the owners’ decision of pursuing further treatment. This study again lacks a histopathological confirmation of HSA but reflects a common situation encountered in clinical practice, where dogs are treated based on a presumptive diagnosis. Although suffering the limitations of a retrospective study, the results suggest a potential advantage in using chemotherapy alone in such cases.

Cyclophosphamide-based metronomic chemotherapy has been used as post-operative adjunctive
treatment in splenic HSA\textsuperscript{101}, showing a similar efficacy when compared to anthracycline-based protocols. Potentially cardiac HSA may be sensitive to the same type of treatment, but again the gross disease setting is not comparable. The authors have treated 2 dogs with cytologically confirmed atrial HSA with a cyclophosphamide-based metronomic protocol, achieving survivals of 20 and 66 days, respectively, with both dogs being euthanased because of recurrence of clinical signs associated with pericardial effusion (unpublished data).

Chemotherapy is the treatment of choice for cardiac lymphoma, as is recommended for other anatomic locations of lymphoma. A small study\textsuperscript{6} on 12 dogs showed that the MST of 5 dogs that received combination chemotherapy (including prednisone, vincristine, cyclophosphamide, L-asparaginase, doxorubicin, mechlorethamine, procarbazine, lomustine) was 157 days. Of the 7 dogs that did not receive any treatment, MST for 6/7 dogs was only 15 days\textsuperscript{6}. In this study, one dog treated with pericardiocentesis only survived \(>1,169\) days, making the original diagnosis questionable. This study also suggested that the prognosis for cardiac lymphoma was not as poor as for other stage V, substage b lymphomas.\textsuperscript{6} This was a very small study, and may also be influenced by clinician/owner bias in advising/declining any further treatment, hence dogs with a worse clinical presentation or more aggressive clinical signs may not have been treated and had a shorter survival.

Future prospective studies may include new targeted therapies such as tyrosine-kinase inhibitors (TKIs), which may have a rationale if used as antiangiogenetic agents, especially in HSA cases\textsuperscript{102}.

For all medical therapies, complete remission is unlikely. Whatever the diagnosis, treatment may also require symptomatic management aimed at controlling tumour bleeding and potential arrhythmias, and other signs caused by the mass effect. Unlike other solid tumours, achieving partial remission (PR) or SD may not lead to adequate control of the associated clinical signs to enhance survival.
Radiotherapy

A single case report\textsuperscript{103} described the use of conformational radiation therapy in a dog with chemodectoma; this resulted in a partial response (more than 50\% reduction in tumour volume). The dog was symptom-free for 32 months, followed by additional 42 months subsequent to additional radiotherapy and pericardectomy. Radiotherapy remains an interesting treatment option to treat heart base masses that are not easily accessible surgically, but more studies are needed to confirm the efficacy of this, and intensity modulated radiotherapy or other highly conformational techniques may be most appropriate.

Cardiac tumours in cats

Cardiac tumours are much less common in cats than in dogs, and tend to be malignant.\textsuperscript{7} One of the largest retrospective studies\textsuperscript{7} reporting 30 cardiac tumours found lymphoma to be the most common. Thirteen cats, 4 of which were FeLV positive, had malignant lymphoma (12 B and 1 T cell). Metastases of extracardiac tumours occurred in the heart in 5 cases. As in dogs, cardiac metastases were predominantly located in the interventricular septum and the left ventricular wall.\textsuperscript{7} Cardiac metastases of a solid adenocarcinoma of the lungs and of mammary adenocarcinomas have also been reported in the same study. A case of a primary pericardial HSA in a 13 year-old domestic shorthair cat with metastases to the liver has also been described\textsuperscript{104}.

Recently pericardial lymphoma has been reported in 7 cats\textsuperscript{105} (1 non-classified, 3 T-cell and 3 B-cell). Diagnosis was confirmed by cytology with fine needle aspirates of the pericardium and cytology of the pericardial and pleural effusions. Clinical findings at presentation may include poor body condition, dehydration and dyspnoea. In most cases, there was echocardiographic evidence of diffuse thickening of the pericardium. Survival time ranged between 7–11 days when untreated or receiving single agent drugs (doxorubicin or prednisolone alone), except for one cat that received a
multi-drug chemotherapy protocol (CHOP protocol) and was still alive 750 days after diagnosis. The long survival time in this case was associated with complete remission confirmed on thoracic radiographs and echocardiography, but the real efficacy of chemotherapy in these cases warrants further investigations.

Achieving stable disease, as in dogs, may not be beneficial for those tumours causing life-threatening clinical signs.

**Conclusions**

Cardiac tumours are rare in dogs and cats and can be challenging to detect. Frequently, a cardiac mass can be identified by echocardiography, however a definitive diagnosis is usually only acquired post-mortem. Sampling of accessible cardiac masses should be considered as this may influence prognosis and treatment, as well as outcome.

Most of the studies reported here are retrospective in nature, limiting the information that can be inferred. A significant sample selection bias has to be suspected, both on the side of veterinarians making treatment recommendations and dog owners. Retrospective studies generally require large sample sizes, in order to yield meaningful results, and many of the studies are on small numbers of cases. Cardiac neoplasms are uncommon in veterinary medicine, and prospective studies are therefore likely to be limited by the slow accrual of cases unless these are very large multicentre studies.

Treatment options are limited, but in cases of HSA best outcomes are achieved with a combination of surgery and chemotherapy (most commonly anthracycline-based). Cardiac lymphoma may respond to multi-agent chemotherapy protocols. However, whatever the diagnosis, treatment often requires symptomatic management of tumour bleeding and potential arrhythmias other than signs caused by the mass effect, as achieving complete remission is uncommon. Unlike other solid
tumours, achieving PR or SD may not lead to adequate control of the associated clinical signs to enhance survival. RT is an interesting but not readily accessible option for heart base tumours. Medical management, beyond adjunctive chemotherapy in HSA, requires further investigation but combination chemotherapy is recommended for lymphoma.

Acknowledgments

The authors would like to acknowledge Dr Jeremy Mortier (Small Animal Teaching Hospital, University of Liverpool, UK) for providing the CT scan images and their description; Dr Ana Canadas (Instituto de Ciencias Biomedicas de Abel Salazar, Universidade do Porto, Portugal) for providing the histopathology pictures and their description; Dr Giorgio Romanelli (Clinica Veterinaria Nerviano, Milan, Italy) for providing the post-mortem and intra-operative pictures.

Brigite Pedro’s cardiology residency training programme was supported in part by Boehringer Ingelheim Vetmedica.

References


50. Aupperle H EC, in March I. Metastasen im Herzen bei Hund und Katze. *Kleintierpraxis* 2012; **57**(7): 357-64


**Figure 1:** Echocardiographic appearance of cardiac masses. A: right parasternal long axis four chamber view, modified to optimise the large and rounded heart base mass located dorsal to the left atrium and right atrium. Cytology of fine needle aspirates of this mass revealed chemodectoma. B: right parasternal short axis view at the level of the heart base, modified to optimise the small and rounded heart base mass. Most likely differential diagnosis: chemodectoma. C: left apical view of the right atrium and right ventricle showing a mass arising from the right atrium and extending into the right atrio-ventricular groove. Cytology of fine needle aspirates of this mass revealed haemangiosarcoma. D: right parasternal long axis view showing a small and mildly heterogeneous mass in the base of the interventricular septum. Cytology of fine needle aspirates of this mass revealed haemangiosarcoma.
Figure 2. (A) Post-mortem appearance of a chemodectoma at the level of the heart base and surrounding the aorta. (B) Post-mortem appearance of a diffuse haemangiosarcoma. Both tumour types have been confirmed on histopathology.
Figure 3: Cytological features of cardiac tumours obtained by fine needle aspiration. Diff-quick stain. A, B: chemodectoma. Note the naked nuclei suggesting a neuroendocrine origin. Marked anisokariosis is also visible (magnification, 100 x). C, D: Haemangiosarcoma. Numerous mesenchymal cells on a background of erythrocytes are visible in figure C (magnification, 20 x). A detail of the mesenchymal cells with basophilic and vacuolated cytoplasm is shown in figure C (magnification, 100 x).
Figure 4: Histopathological features of cardiac tumours. A: Haemangiosarcoma. Spindle to polygonal cells with indistinct cytoplasmic limits arranged in interlacing bundles enclosing blood-filled spaces. (H&E, original magnification 400x) B: Chemodectoma. Tumour polygonal cells are arranged in nests and packets supported by a fine and delicate fibrovascular stroma (H&E, original magnification 100x).
Figure 5: CT appearance of a chemodectoma. Oblique (A) and transverse (B) post-contrast thoracic CT at the level of the aortic root. There is a large, well marginated, irregularly shaped, heterogeneous and hypoattenuating mass dorsal to the aortic root, displacing the heart ventrally. The image B shows the mass in the plane of the aortic root. Note the ventral and left-sided displacement of the aorta. R: right, L: left; Ao: aorta; C: cardiac silhouette; T: trachea; M: mass.

Figure 6. (A) Intraoperative view of a right atrial haemangiosarcoma (HSA). (B) Right auricular appendage HSA before surgical excision.