Cardiac or Non-Cardiac Cough Clues to Distinguish

Leah A. Cohn, DVM, PhD, DACVIM (SAIM)
Professor, Department Veterinary Medicine and Surgery, College of Veterinary Medicine, University of Missouri, MO, USA
Notes were co-written by Dr. Deborah Fine, DVM, MS, DACVIM (Cardiology) for a prior joint presentation.

INTRODUCTION

Coughing is a common presenting complaint seen with both respiratory and cardiovascular disease. Coughing is a normal protective reflex that occurs when cough receptors located throughout the respiratory tract are stimulated. The reflex allows for the expulsion of mucus, particulates and infectious agents to protect the lungs. However, the protective reflex is not always sufficient to result in self-cure, or occurs when irritation of receptors is due to disease not associated with particulates or infection. A very similar but distinct process results when laryngeal receptors are irritated, resulting in "huffing" noise that few owners will be able to distinguish from a cough. With few exceptions, cough is due to disease of either the airways, the lungs, or the heart. It can be challenging to distinguish between cardiogenic and non-cardiogenic causes of coughing, but this distinction is crucial for appropriate diagnostic planning and for appropriate treatment. Adding to the frustration of trying to distinguish between these causes of cough, the very animals predisposed to myxomatous degenerative mitral valve disease (a common cardiac cause of cough) are also predisposed to some of the most common non-cardiogenic causes of cough (e.g., tracheal collapse, chronic bronchitis).

The most frequent causes of cardiogenic cough are left-sided congestive heart failure with pulmonary edema, and left mainstem bronchial compression secondary to left atrial enlargement. The most common causes of heart failure in the dog are chronic myxomatous degenerative valve disease (endocardiosis) and dilated cardiomyopathy. Less commonly, dogs with arrhythmias may also present with coughing. The mechanism of this is poorly understood, but may relate to excessive motion of the heart stimulating pulmonary C fibers. Congestive heart failure in the cat does not cause coughing. Coughing in feline patients is almost invariably due to underlying pulmonary or airway disease such as asthma, bronchitis, or heartworm disease. Therefore, this presentation will focus on cough in dogs.

Non-cardiac causes of cough are much more numerous than cardiac causes. Airway diseases are often divided anatomically into upper or lower airway disorders. Although occasionally nasal disease results in cough in animals when nasal discharge drips backwards into the nasopharynx or irritates the larynx, disorders such as infectious tracheobronchitis, collapsing trachea, or foreign bodies are more common causes of upper airway cough. Airway (trachea and bronchial) collapse, chronic bronchitis, pulmonary parasites, and non-parasitic airway eosinophilic disease are common lower airway causes of cough. Nearly all types of lung disease, including infectious and non-infectious pneumonia/pneumonitis, primary and metastatic neoplasia, non-cardiogenic pulmonary edema, and various interstitial lung diseases such as pulmonary fibrosis may result in coughing. Although animals with pleural space disease may also cough, this is likely due to irritation of the adjacent lung tissue rather than from pleural disease itself.

PHYSICAL EXAMINATION

A thorough physical examination will often provide clues to the underlying disease process. A dog with no signs of cardiac disease on physical examination (e.g., no heart murmur, arrhythmia or abnormal heart sounds [gallops, clicks, split S1 or S2 heart sounds]) is extremely unlikely to have heart disease as the cause of the cough. On the other hand, the presence of abnormal heart sounds does not rule-out primary respiratory disease as the cause of cough, as these may be incidental findings. Animals with congestive heart failure have high sympathetic tone and are thus almost invariably tachycardic on presentation. The absence of tachycardia in a patient with coughing or respiratory distress, regardless of the presence of a murmur, usually rules-out heart failure. In the same way, sinus arrhythmia is often pronounced in

animals with lung or airway disease but is unlikely in animals with cardiogenic cough. Other clues to discriminate between cardiogenic and non-cardiogenic cough can be found on auscultation. Although audible crackles accompany both cardiogenic and non-cardiogenic causes of cough, ventral or unilobar crackles would tend to support non-cardiogenic cough while diffuse or perihilar crackles are more typical of cardiogenic cough. Extremely harsh, loud crackles throughout the lungs when a radiographic alveolar infiltrate is lacking are highly suggestive of pulmonary fibrosis. Since pulmonary fibrosis can lead to pulmonary hypertension, these dogs often have a right sided heart murmur that can make it easy to mistake them for having heart failure. Neither wheezes nor stridor are associated with cardiogenic causes of cough, and would instead suggest lower or upper airway disorders, respectively.

IMAGING STUDIES

Thoracic radiography is an invaluable diagnostic test to help ascertain the cause of cough. Additionally, serial thoracic radiographs are useful for determining response to therapy and progression of disease.

At least two orthogonal views should be obtained (i.e., a lateral and either a ventrodorsal (VD) or dorsoventral (DV) view) at peak inspiration to evaluate the lungs and heart, while expiratory films are needed to identify intra thoracic tracheal collapse. Differences in the radiographic appearance of thoracic structures exists between the left and right lateral projections and between the VD and DV projections, with one view being preferred over the other depending on the clinical situation. In the DV position, the heart is suspended in its normal orientation and is closer to the sternum. The DV view also allows more easy visualization of the caudal lobar pulmonary vessels. In the DV position, the dorsal lung fields are more inflated and the air provides increased contrast with the vessels. Further, in this orientation the caudal vessels are more perpendicular to the x-ray beam, and the vessels are farther from the table top and are therefore more magnified. On the VD view, the shape of the cardiac silhouette is more variable. The right heart may appear prominent, taking on a "reverse D" appearance. The viewer should be careful not to over interpret this as right heart disease. Small volumes of pleural effusion are often better visualized on the VD. Magnification of the ventral lung fields improves pulmonary parenchymal evaluation. For optimal visualization of pulmonary nodules, all four orthogonal views should be obtained.

Although the terms "heart" and "cardiac silhouette" are used interchangeably, it is important to remember that this structure on a radiograph simply represents the overall size of the pericardium and its contents. If the cardiac silhouette is interpreted as enlarged, then the next question becomes "what is causing the enlargement"? Differentials would include an actual increase in the size of the heart, presence of pericardial effusion, neoplastic mass, or herniation of abdominal contents into the pericardium (peritoneal pericardial diaphragmatic hernia). Frequently, additional imaging is necessary to make a final determination.

On lateral views, the heart width typically spans 2.5 to 3.5 intercostal spaces. The height of the heart from apex to the carina should be $\leq 2/3$ of the height of the thoracic cavity. On DV/VD views, the maximal width of the heart should be $\leq 1/2$ the width of the hemi-thorax at the 9th rib. A vertebral heart scale (VHS) system was developed to provide a more objective determination of cardiac size. Using the lateral view, the long and short axes of the heart are measured. The measurements are then superimposed over the vertebral column, both starting at the cranial edge of T4, and the number of vertebrae covered is then summed. Normal dogs have a VHS of 8.5 to 10.6 although there are some breed variations with Boxers, Labradors and Cavaliers having normal VHS up to 12. Normal cats have a VHS of 7.2 to 7.8. A combination of these methods should be used to fully interpret the cardiac size.

Specific chamber enlargement can also create abnormalities in the cardiac silhouette. In lateral views the cranial aspect of the cardiac silhouette is composed of the right atrium and ventricle, while the caudal aspect is composed of the left atrium and ventricle. The cranial dorsal region, the "cranial cardiac waist", is composed of three overlapping structures: the right atrium, pulmonary artery, and aorta. Loss of the cranial cardiac waist can be due to enlargement or dilatation of any of these cardiac structures and evaluation of the orthogonal view is necessary to determine which is involved. The caudal dorsal region, the "caudal cardiac waist", is composed only of the left atrium. Serial radiographs to assess for left atrial enlargement are very useful for monitoring for progression of degenerative mitral valve disease in dogs.

In cats, left atrial enlargement is best appreciated on the DV/VD projections. Left atrial enlargement causes widening of the heart base, commonly referred to as a valentine-shaped heart.

A clock-face analogy is commonly used to identify cardiac structures on the DV/VD view. The aortic arch is positioned from approximately 11:00–1:00 o'clock; the main pulmonary artery is from 1:00–2:00; the left auricle is from 2:00–3:00; the left ventricle is 3:00–6:00; the right ventricle is 6:00–9:00; and the right atrium is 9:00–11:00. The left atrium is central and just caudal to the bifurcation of the mainstem bronchi.

Evaluation of the pulmonary vasculature is crucial for distinguishing between causes of respiratory signs. On the lateral projections, the pulmonary vasculature is best visualized in the cranial lung fields. The pulmonary arteries are dorsal and the veins are ventral. On DV/VD projections, the pulmonary vasculature is clearest in the caudal lung fields with the pulmonary arteries are lateral and the veins medial. The pulmonary artery and veins should be symmetrical, and on the lateral projection their width should ≤ to the width of the 4th rib. On DV/VD views, they should be ≤ to the width of the 9th rib.

Enlargement of the pulmonary arteries is implicative of pulmonary arterial hypertension. Depending on the region of the country, heartworm disease should be at the top of your differential list with this finding. Primary pulmonary disease (e.g., COPD, asthma, bronchitis, pulmonary fibrosis, etc.) can also cause pulmonary hypertension with resulting arterial enlargement. Enlargement of the pulmonary veins is a hallmark feature of congestive heart failure and is results from increased left atrial and ventricular diastolic pressure. Symmetrical enlargement of both the arteries and veins indicates a combination of pulmonary hypertension and increased left atrial pressure. In a young animal, this is most likely due to a left-to-right shunting cardiac defect. In an older animal, this is most likely due to a combination of left heart failure, and either primary pulmonary disease or pulmonary hypertension secondary to chronically increased left atrial pressure (e.g., chronic degenerative mitral valve disease).

Evaluating the pulmonary parenchyma and airways for specific lung patterns is useful in distinguishing between cardiac and non-cardiac causes of cough. In most cases, when radiograph abnormalities are seen in the lung fields, a prioritized list of differential diagnosis is possible but more invasive tests, such as alveolar lavage, are usually necessary to determine the specific lung disease present. It is also important to remember that non-cardiogenic causes of cough may be present with a radiographically normal thorax (both heart and lungs). For example, thoracic radiographs have only modest sensitivity for two of the most common causes of chronic non-cardiogenic cough in dogs - chronic bronchitis (50–60%) and tracheal collapse (60–70%). Similarly, acute cough associated with tracheobronchitis, pulmonary thromboembolism, acute aspiration, etc, may not cause any imaging abnormalities.

Besides the vascular patterns, other radiographic lung patterns are described as interstitial, alveolar, bronchial, or a combination of these. Interstitial patterns can be structured (e.g., nodular) or unstructured. Unstructured interstitial pattern shows an increase in lung opacity with all normal structures still visible, but with hazy margins. This pattern results from accumulation of fluid or cellular material in the interstitial spaces, and is one of the most commonly recognized patterns and not particularly helpful in making a specific diagnosis. It can even be seen in animals with early edema or pneumonia. Nodular interstitial patterns are typical of fungal pneumonia, neoplasia, or eosinophilic bronchopneumopathy. Often, the nodules seen in fungal pneumonia are smaller and of a more uniform size (described as a miliary interstitial pattern) than the variably sized nodules of metastatic cancer. Primary lung cancer often shows up as a single large nodule in the caudal lung fields.

An alveolar pattern is characterized by complete loss of margins of the pulmonary vasculature, and the presence of air bronchograms (a uniform soft tissue opacity surrounding the radiolucent bronchus). An air bronchogram is caused by fluid filling the terminal alveoli. Alveolar patterns can occur with pulmonary edema, pneumonia (aspiration or infectious), hemorrhage, atelectasis, lung lobe torsion or neoplasia. The location of the alveolar pattern can be helpful in that edema due to congestive heart failure is usually perihilar in the dog, while bacterial pneumonia is ventral, and aspiration pneumonia is often found in the right middle lung lobe or the caudal portion of the left cranial lobe.

A bronchial pattern is caused by thickening of the airways, either from inflammation or mineralization of the airways themselves (e.g., asthma, bronchitis) or interstitial fluid tracking along the airway margins. Radiographically this appears as "donuts" and "tramlines".

Early cardiogenic pulmonary edema appears as interstitial to bronchointerstitial infiltrate. As failure worsens the interstitium becomes saturated, causing the fluid to fill the alveoli. Cardiogenic edema is typically bilaterally symmetrical. In the dog it is most prominent in the caudodorsal and perihilar regions. In cats, it is typically found in the ventral regions, although a diffuse distribution can also be seen. Large volume pleural effusion as a manifestation of heart failure is much more common in cats than in dogs.

In summary, left-sided congestive heart failure is diagnosed by the presence of three radiographic signs: 1) left atrial enlargement, usually accompanied by left ventricular enlargement; 2) distention of the pulmonary veins (with or without pulmonary arterial distension); and 3) interstitial to alveolar pattern in a location consistent with heart failure for the species. In order to make the diagnosis of heart failure, all three of these signs should be present. Any radiographic pattern, including normal lungs, is possible in the presence of lung or airway disease. While the lung pattern can allow differentials to be ordered, they seldom allow definitive diagnosis of respiratory disease.

BIOMARKERS

Occasionally results of routine blood tests provide clues as to the cause of cough. More useful in distinguishing between cardiac and pulmonary causes of cough and respiratory distress are specific biomarkers such as natriuretic peptides and troponins.

Natriuretic peptides are a family of structurally related hormones that include atrial and B-type natriuretic peptides (ANP and BNP). These hormones exert a variety of effects to maintain circulatory homeostasis in states of increased extracellular volume. They promote natriuresis, increase glomerular filtration rate, induce peripheral vasodilation, and act as antagonists of the renin-angiotensin system. Studies of dogs with experimental and naturally occurring heart disease have shown that ANP and BNP increase proportionally to the severity of heart disease and clinical signs of heart failure. ANP is primarily released by the atria in response to stretch. A small amount of BNP is released by the atria in response to distention, but the majority of BNP is released by the ventricle. A variety of cardiac disease states have been associated with increased BNP including systolic dysfunction, diastolic dysfunction, volume overload, and pulmonary hypertension

Natriuretic peptides are initially synthesized as pro-hormones which are enzymatically cleaved to the active fragments (ANP and BNP) and the inactive amino-terminal fragments (NT-proANP and NT-proBNP). The active fragments are rapidly metabolized and have quite short half-lives compared to the inactive fragments. Both markers have been shown to be useful for the detection of heart failure and discrimination of non-cardiogenic respiratory distress. BNP, but not ANP has been found to detect heart disease in the early asymptomatic stage.

In the United States only NT-proBNP is readily available as a diagnostic test (CardioPet; IDEXX Laboratory). In general, if the NT-proBNP result is normal or only slightly increased in an animal with respiratory signs, this rules out a cardiogenic cause. However, if an animal with signs of respiratory disease has an increased NT-proBNP it does not automatically follow that the cause must be heart failure. An animal with significant concurrent cardiac AND respiratory disease will have an increase in NT-proBNP and therefore, this test must be used in conjunction with radiographs and possibly echocardiography.

Cardiac troponins regulate the interaction between actin and myosin during excitation-contraction coupling. Cardiac troponin I (cTnI) is a sensitive marker for myocardial ischemia and necrosis, and is released into circulation response to sarcomeric injury. In human medicine cTnI is used routinely for the detection of myocardial infarction, a condition that is exceedingly rare in dogs. Cardiac troponin I was elevated in dogs with dilated cardiomyopathy and degenerative mitral valve disease compared to healthy dogs with no echocardiographic evidence of heart disease. Further, this study showed that cardiomyopathic dogs with cTnI levels > 0.20 ng/ml had a median survival less than half that of dogs with cTnI < 0.20 ng/ml (112 days versus 357 days). Utility for this test in distinguishing cardiogenic from non-cardiogenic cough remains to be determined.

REFERENCES

References are available upon request