Polyunsaturated fatty acids in canine heart disease
Executive summary: omega-3 in heart health in dogs

Ten percent of the dog population are currently estimated to be affected by heart disease; ninety percent of which suffer from mitral valve disease (MVD) or dilated cardiomyopathy (DCM); both incurable and progressive diseases.

From the onset of both these conditions, there is a long "preclinical" phase, during which the dogs have no clinical signs of heart failure and appear to be healthy. During this phase dogs of certain breeds have an increased risk of cardiac arrhythmia.

Adaptive mechanisms in the vascular system and the heart compensate for the reduction in cardiac output. These compensatory mechanisms lead to cardiac remodeling and may contribute to the worsening of cardiac function. Human studies have indicated that inflammation and changes in myocyte metabolism may play an important role in this part of disease progression.

As there are no pharmaceutical drugs shown to be effective during this phase, the vets may try to support the heart by suggesting dietary changes and exercise.

In humans, there is good evidence that two of the omega-3 fatty acids, eicosapentanoic acid (EPA) and Docosahexaenoic acid (DHA), can help support heart health. In dogs, there is also some evidence that EPA and DHA, can help support heart health. Mechanisms through which EPA and DHA are believed to be of benefit involve reduction of inflammation, support of myocyte metabolism and cell membrane stabilisation.
Cardiac disease in dogs

Ten percent of dogs in the general population are estimated to have heart disease. This is expected to rise as longevity is increasing; with obese dogs and certain breeds being particularly at risk.¹

Of the affected population of dogs with heart disease, ninety percent are diagnosed as either having mitral valve disease (MVD) or dilated cardiomyopathy (DCM).¹² Both diseases are chronic and progressive with no curative treatment at present.²

Mitral Valve Disease (MVD)

MVD is a disease characterised by an initial denudation of the endothelium on the mitral valves leading to incompetence of valves due to a gradual thickening caused by a build up of collagenous material.¹ In this environment, genes involved in the inflammatory response are upregulated indicating that there may be an inflammatory component to valve deterioration.⁴ This is supported by recent research which has demonstrated an increased level of inflammatory mediators.⁵

As the valves become incompetent the decreased output from the heart leads to stimulation of the sympathetic nervous system, which increases the heart rate and contractility, and increases water retention in the kidneys to expand plasma volume.² Over a period of time the compensatory mechanisms contribute to a gradual enlargement of the heart; recognised macroscopically as cardiac remodeling.²

The compensatory mechanisms may allow the patient to remain free of clinical symptoms and is therefore unpredictable.² The time from diagnosis of disease to development of clinical signs of the disease is often several years.⁶ These signs appear when the compensatory mechanisms are no longer able to maintain proper blood circulation.²

Dilated Cardiomyopathy (DCM)

DCM is characterised by a gradual weakening and elongation of the heart muscle cells. These changes cause gradual dysfunction of the myocardium leading to a progressive failure of the heart to pump blood efficiently. As in MVD, the decrease in pump function leads to a stimulus of the sympathetic nervous system and chronic activation of the sympathetic nervous system followed by a gradual enlargement of the heart.²

Dogs with DCM can remain free of clinical signs of disease for many years. But it has been shown that in certain breeds, some dogs have an increased risk of sudden death due to cardiac arrhythmia.⁷

Once the DCM dog has clinical symptoms of the disease, disease progression is rapid and some studies have shown that more than half of dogs die within the first year after onset of clinical symptoms.⁸
Role of inflammation in decompensated cardiac disease

Inflammation is believed to be a significant factor in progression of human chronic heart failure. This inflammation is characterised by an increase in pro-inflammatory cytokines such as TNFα, IL1 and IL6, believed to be produced by cells such as myocytes in response to cellular stimulation (including cell damage). In experimental models of heart failure, increased activation of TNFα, has been linked to increased inflammation, decreased contractility of cardiac tissue and increased rate of remodeling. Elevated levels of pro-inflammatory cytokines have been found to be associated with an increased risk of cachexia.

There are not many studies investigating effect of inflammation in dogs with heart disease, however one study found a negative correlation between the levels of pro-inflammatory cytokine IL1 and survival time.

In the normal heart, myocytes efficiently metabolise fatty acids to meet their energy requirements. In the heart affected by chronic heart failure, myocytes are believed to undergo complex changes in the metabolic pathways, which reduce their ability to produce energy efficiently. Such changes have been found to be associated with myocyte damage and increased apoptosis and there is some evidence that this may play a role in the remodeling process of the heart.

Thus, there is a growing body of evidence that reducing inflammation could therefore be an important step in maintaining heart health.

What are polyunsaturated fatty acids?

Polyunsaturated fatty acids (PUFAs) are essential elements of the cell membrane important for regulation of cellular function.

The two types most often mentioned in relation to health are:

- Omega-3 fatty acids
- Omega-6 fatty acids

Of these PUFAs, increased intake of two omega-3 types, eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA), has been found to be related to reduction in incidence of cardiovascular events in humans and to an increase in survival in dogs with heart failure.
Dietary sources of EPA and DHA

Mammals are not able to synthesise the omega-3 PUFAs and they therefore depend upon a sufficient consumption of these fatty acids from the diet in order to meet their physiological requirements.16

The concentrations of the omega-3 PUFAs EPA and DHA in the human and dog diet are usually very low. Diets that are low in EPA and DHA can be improved by supplementation.

Replacement of AA by EPA/DHA

Increasing the amount of EPA and DHA in the diet increases their concentration in the cell membrane as they readily displace the omega-6 fatty acid arachidonic acid (AA)

Effects of EPA and DHA in heart health

In humans, there is good evidence that two of the omega-3 fatty acids, EPA and DHA, can help support heart health.14 This evidence has been implemented in guidelines for management of heart health in humans to the extent that daily omega-3 supplementation is now recommended.

There are indications that the observed reduction in the incidence of cardiovascular events in humans may be the sum of many effects of EPA and DHA, some of which might also be relevant in canine heart disease. These include the ability to reduce the production of pro-inflammatory cytokines, TNFα and IL1 in patients with heart failure,17 the ability to modulate the excitability of myocytes through the direct interactions with membrane ion channels and the ability to attenuate pressure overload-induced remodeling, and contractile dysfunction.19
Reduction of inflammation

When myocytes are damaged the fatty acids in the cell membrane are released as precursors for inflammatory mediators. The type of inflammatory mediator which is produced depends upon the type of fatty acids from which it originates.

Those inflammatory mediators which are produced from EPA and DHA are less inflammatory than those mediators, which are produced from other types of fatty acids. This is supported by studies that demonstrate that increasing the dietary intake of EPA and DHA may reduce the concentration of pro-inflammatory mediators.\textsuperscript{12,20}

Heart cells (Myocytes)

- EPA and DHA
- Other fatty acid
- Cell injury

**No supplementation with EPA/DHA**

- Each myocardial cell membrane is made up of thousands of fatty acids
- When the cell is injured, signaling increases. The type of response to the signal will depend on the ratio of the different types of fatty acid
- Release of inflammatory mediators
- Initiates and drives inflammation
- Increases rate of cardiac disease progression

**Supplementation with EPA/DHA**

- Release of less inflammatory mediators
- No increase of inflammation
- Does not contribute to further disease progression
Other supportive effects of EPA and DHA supplementation in heart disease

Support of myocyte metabolism

EPA and DHA are believed to support myocyte metabolic efficiency through up-regulation of the expression of lipid metabolism genes. Increased intake of EPA and DHA has been associated with decreased cachexia score and increased survival in two studies in dogs with heart failure.

Decreasing risk of arrhythmia

In dogs, EPA and DHA have been linked to decrease of ventricular fibrillation after induced cardiac arrhythmia in experimental models and to reduction of arrhythmia in boxer dogs with arrhythmogenic right ventricular cardiomyopathy in a clinical study.

Support of canine heart health with EPA and DHA

There are currently no pharmaceutical drugs that have been proven to be beneficial in the preclinical phase of heart disease. Therefore, vets may support the heart during this phase by suggesting dietary changes and exercise. There is some documentation that increasing EPA and DHA intake in dogs with heart disease may support compromised hearts. Supplementing dogs with heart disease with EPA and DHA may be one of the management options for support of heart health.
Reference List